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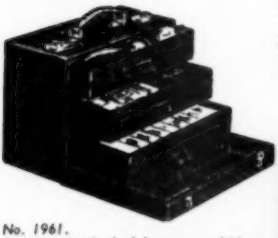

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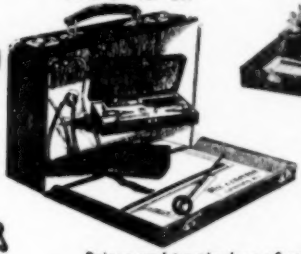

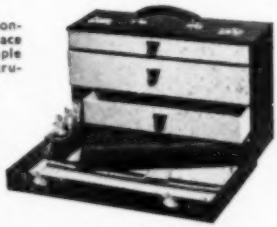

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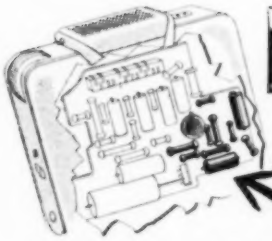

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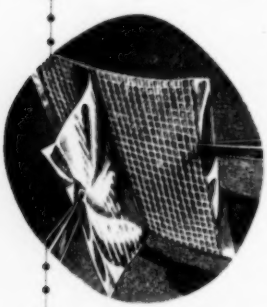

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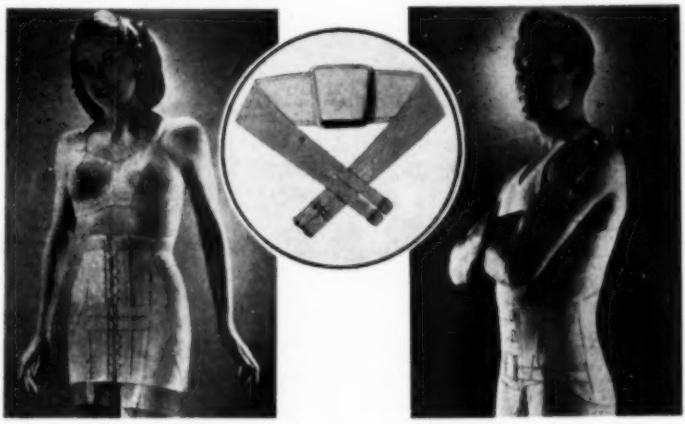

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for peripheral vascular disease

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ULCERS OF THE LEG
RAYNAUD'S PHENOMENA
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NOCTURNAL CRAMPS
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ISCHAEMIA OF THE FEET
POST-PHLEBITIC SYNDROME
INTERMITTENT CLAUDICATION
DYSMENORRHOEA
CHILBLAINS

FREE FROM SIDE EFFECTS

now available to the Medical Profession

★ References:- BRITISH MEDICAL BULLETIN, 1952. Volume 8. No. 4. p. 373
BRITISH ENCYCLOPAEDIA OF MEDICAL PRACTICE, 1952. Volume 11, page 637.

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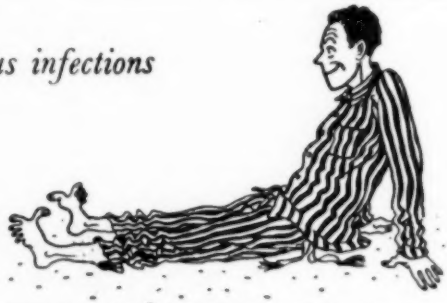
'Sopronol' for fungous infections of the feet



'SOPRONOL' Ointment fulfils the criteria laid down* for the ideal fungicidal compound :

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IT PENETRATES THE STRATUM CORNEUM, REACHING THE DEEP SEATED MYCELIA

IT NEITHER IRRITATES NOR SENSITIZES THE SKIN

This therapeutic efficiency derives from the use of *Sodium Propionate* and *Caprylate* — both originally isolated from concentrated human sweat. It is this physiological kinship which enables 'SOPRONOL' to control the most chronic case of *Tinea Pedis* . . . with a complete absence of the superadded skin sensitisations so liable to complicate treatment.

* Bulletin Johns Hopkins Hospital, (1944), 75, 417.

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the balanced formula being both antispasmodic and sedalgesic affords rational therapy in dysmenorrhoea and other psychosomatic problems.

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offer oestrogen therapy plus safe sedation and provide for complete relief of menopausal symptoms.

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"CPL" preparations are not advertised to the public and may be freely prescribed.

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1 oz. tubes (Undecylenic acid 5%—zinc salt 20%)

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ELIXIR GABAIL

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The urgency of treatment for Burns and Scalds is well supported by BORNOLIN

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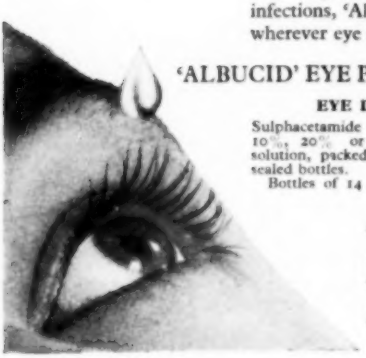

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75 i.u. per gelucap *Bioglan*

For CARDIOVASCULAR-RENAL DISEASES

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PROCAINE PENICILLIN G
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DIHYDROSTREPTOMYCIN SULPHATE

Not infrequently,
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require immediate treatment
and to await proper bacteriological examination
may be quite impracticable or inadvisable.

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'Distavone', consisting of a balanced mixture of
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in a highly purified form,
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Each single-dose injection-type vial contains 300,000 units procaine penicillin G, 100,000 units potassium penicillin G and 500,000 units (equivalent to 0.5 gramme pure base) dihydrostreptomycin sulphate. Boxes of 5 vials.

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This improvement in mood is of outstanding value in a disease where the influence of the mind over the body is so marked. It beneficially alters the reaction to pain and lessens the patient's preoccupation with his symptoms. Dose: 2 tablets repeated three hourly as necessary.

'Edrisal' *the dual-action analgesic — relieves pain — elevates mood*

Available on prescription in bottles of 25 tablets

Each 'Edrisal' tablet contains:
Amphetamine ('Benzedrine') sulphate . . . . . 2·5 mg
Acetylsalicylic acid . . 160 mg.
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Only 'Neophryn' combines powerful action—(equal 1 to 3% ephedrine)—with low toxicity.

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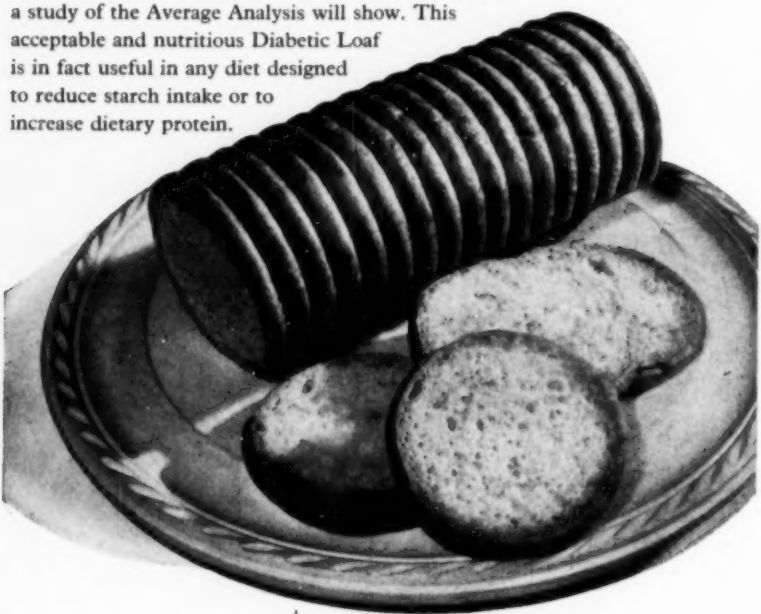

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One ounce of this bread at 30% moisture content contains:—

Protein	6.5 grams
Mineral matter ...	0.5 grams
Fat	2.5 grams
Carbohydrates ...	10.5 grams
Protein-Carbohydrate ratio ...	1 to 1.6 approx.
Carbohydrate content per slice ...	*2.5 grams approx.*

DESIGNED FOR EASY MEASUREMENT

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- **is non-greasy, and easily removed by rinsing.**
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'CETAVLEX' Cream

Trade Mark (contains 'Cetavlon' Cetrimide B.P.)

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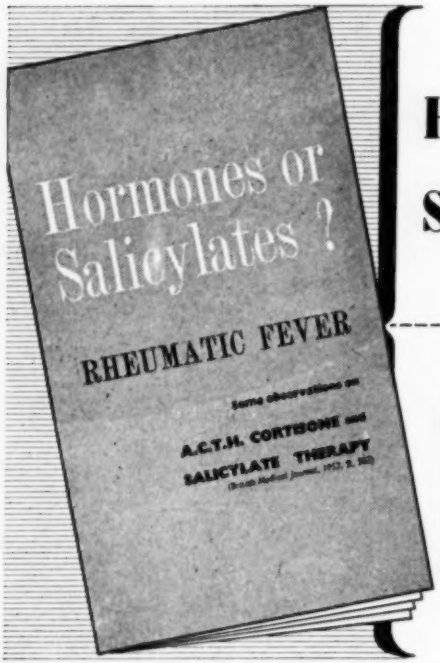

HORMONES OR SALICYLATES ?

Rheumatic Fever

Some observations on

A.C.T.H., CORTISONE and

SALICYLATE THERAPY

(British Medical Journal, 1952, 2, 582)

IN 1951 we published and distributed amongst the Medical Profession a booklet entitled 'The Similarity in the Mode of Action of Salicylates and Cortisone in the Treatment of Rheumatism'.

It is interesting to note the report of the treatment of Rheumatic Fever published in the British Medical Journal (1952, **2**, 582) which provided evidence that salicylates (in the form of Berex) act in a similar manner to A.C.T.H. An abstract of this report is now available in booklet form on request.

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for the relief of symptoms associated with all rheumatic disorders.

FORMULA: *Each tablet contains Calcium Succinate, 2.8 gr., Acetylsalicylic Acid 3.7 gr.*

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relieves symptoms
eliminates discharge
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in non-specific leucorrhea following cervical cauterisation following vaginal plastics in routine postpartum care

*Triple Sulfa Cream : Sulphathiazole N'Acetylsulphanilamide, N'Benzoylsulphanilamide with urea peroxide

On original prescriptions specify "Triple Sulpha Cream with applicator"

To restore and maintain normal acidity

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IN RECURRENT VAGINITIS

Restoration of normal acidity is important in preventing recurrence of vaginal infection. Recurrence is especially marked in trichomoniasis and often a problem in moniliasis. Highly buffered Aci-jel (pH. 4.0) is unexcelled for restoring normal acidity. It is simply applied, prolonged in action and non-irritating.

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'Milk of Magnesia' reacts with the acids of the stomach to form a neutral laxative salt which promotes gentle but effective elimination.

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mental and emotional distress

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a balanced combination of 'Dexedrine' and amylobarbitone

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the tonic——

COLLOTONE

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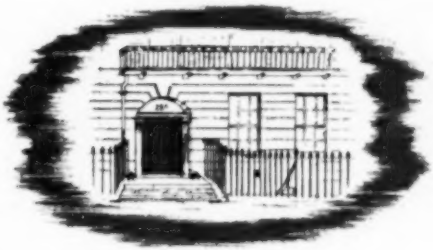
These services are offered entirely free of charge and you are invited to apply for further details to the Energen Dietary Service.



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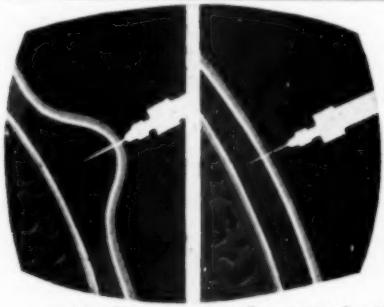


Local anaesthesia

'WYDASE' (freeze-dried Hyaluronidase) enhances the *speed* and *depth* of local anaesthesia, increasing the anaesthetic area by 40%. It is recommended for use in GENERAL SURGERY, and in ORTHOPAEDIC SURGERY for the infiltration of sprains or reduction of simple fractures such as the Colles. The freedom from tissue distortion following its use in PLASTIC SURGERY enables appraisal of results during the progress of the operation.

300 T. R. units of 'WYDASE', freshly dissolved in 1 c.c. of cold sterile normal saline, should be added to 50 c.c. of cool anaesthetic solution containing 0.5 c.c. of 1 : 1000 adrenaline.

'WYDASE'
Trade Mark
FREEZE-DRIED HYALURONIDASE

Wyeth

John Wyeth and Brother Ltd.
Clifton House, Euston Road, London, N.W.1

PROTEIN DEFICIENCY AND THE VALUE OF

BROCKHAM

HIGH PROTEIN FOOD

Brockham High Protein Food added to the diet provides the extra protein needed by so many patients. This extremely valuable nutritional supplement contains over 21% of first class protein all derived from rich unspoiled sources, together with the "trace" elements and B-Complex Vitamins of the constituents. The health-giving properties of Brockham High Protein Food are *enhanced* when they are combined in this concentrated form.

BROCKHAM HIGH PROTEIN FOOD

is a concentrate of

★ **POWDERED BREWERS YEAST**

★ **YOGHOURTED SKIM MILK**

★ **MOLASSES**

★ **WHEAT GERM**

In addition to first class Protein, Brockham Food contains B-Complex Vitamins and "trace" elements from unspoiled natural sources.

We shall be glad to send you a sample packet on request within the U.K.

Obtainable from all Chemists and Health Food Stores everywhere. 3/- and 5/6

BROCKHAM FOOD LABORATORIES LTD., ACTON LANE, LONDON, N.W.10

MI/Y

New Peptic Ulcer Treatment Comparable to Drip Therapy

Whole milk and alkaline constituents combine to produce increased buffering action

NULACIN TABLETS have been evolved to meet a very real need in the treatment of gastric and duodenal ulcers.

All the literature on the treatment of peptic ulcers emphasizes the proven value of diminishing the acidity of the gastric juice. Many large and otherwise intractable ulcers can be healed by a continuous, intra-gastric drip of milk or alkali.

Drip therapy is, however, not always available or practicable to use in many instances. Nulacin offers a satisfactory alternative.

CONTINUOUS NEUTRALIZATION

NULACIN TABLETS, allowed to dissolve slowly in the mouth, have been shown clinically to provide a continuous neutralization comparable with that of drip therapy. (B.M.J., 1952, 2, 180.)

NULACIN TABLETS contain nutrient in a most acceptable form to the peptic ulcer patient. They obviate the necessity of taking frequent feeds, and so lessen the tendency to obesity in those following a dietary regime of food at frequent intervals.

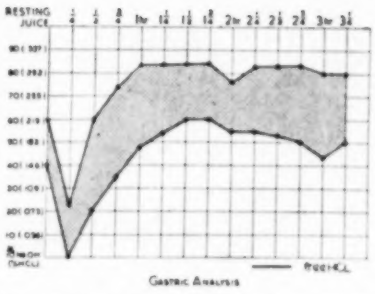
During ulcer activity the suggested dosage is 3 tablets to be sucked each hour, and for follow-up treatment 2 tablets should be sucked between meals, beginning half an hour after a meal.

The tablet is of a suitable size, and of a consistency and hardness, so that, when it is sucked, the result is a constant and prolonged neutralization of the gastric juice.

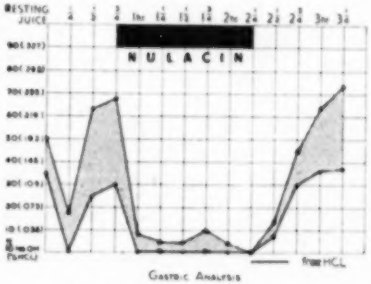
NULACIN TABLETS during extensive clinical tests proved to be extremely palatable and particularly acceptable to patients.

The patient should be instructed to place the tablet between the gum of the upper jaw and the cheek. Here it will be comfortable, and slowly dissolve. The efficacy of the tablet is greatly diminished if it is chewed and swallowed.

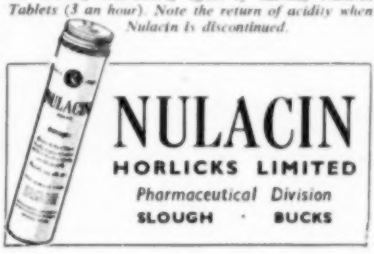
NULACIN TABLETS are not advertised to the public. There is no B.P. equivalent to this tablet. The dispensing pack of 25 tablets is free of Purchase Tax. Price to pharmacists 2/-.



Superimposed gruel test-meal curves of six patients with duodenal ulcer.



The same patients as in Fig. 1, two days later, showing the striking neutralizing effect of sucking Nulacin Tablets (3 an hour). Note the return of acidity when Nulacin is discontinued.



Gastro-Duodenal Ulceration

Rapid disintegration ensures prompt relief from Epigastric pain due to hyperacidity and gastro-duodenal ulceration
A prolonged "buffering action" for over three hours is established causing no "acid rebound."
The liberation of the amino acid glycine stimulates the granulation of the ulcer bed and the normal enzyme activity is ensured whilst the mucosa is protected by the freely formed colloidal gel.

The Medical Management of Gastro Duodenal Ulceration

FORMULA: *Dihydroxy aluminium aminoacetate 250 mgms; Glycine—30 mgms.*

PACKS: *Bottles of* 100 *tablets*—84/- *(doz.): Bottles of* 1000 *tablets*—62/- *(each). (Prices plus P. Tax).*

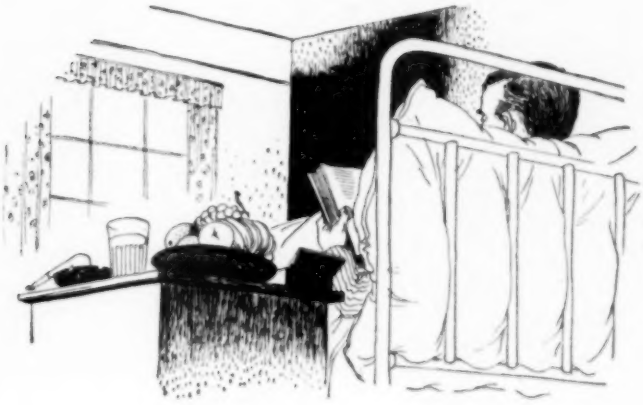
Ref.: Med. World
Vol LXXVII
Sept. 12, 1952

TABNET BRAND
DIHYDROXY
ALUMINIUM AMINOACETATE

Literature available on request from the Medical Department

CALMIC LIMITED · CREWE HALL · CREWE · TEL. 3251-5

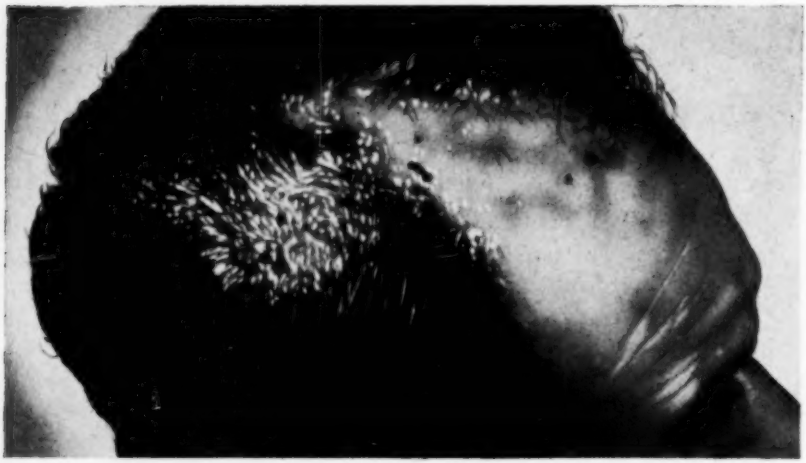
In convalescence



Lethargy and loss of appetite—the very conditions which, in convalescence, it is essential to reverse—are also among the earliest symptoms of Vitamin B deficiency. The administration of B-complex Vitamins to convalescent patients is, therefore, common expedience. 'Beplex,' an established means of providing a balanced dosage of the important B Vitamins, naturally prepared, may be accepted with equal confidence for specific therapy or prophylaxis. It is available as an agreeable elixir or in capsule form to suit the preference of the patient.

'Beplex'
TRADE MARK
ELIXIR & CAPSULES

JOHN WYETH & BROTHER LIMITED Wyeth CLIFTON HOUSE, EUSTON RD., N.W.1



In Seborrhoeic Dermatitis

. . . involving the scalp, face, sternal, interscapular regions, or the areas behind the ears, 'Pragmatar' is widely used and recommended.

'Pragmatar' incorporates in a superior oil-in-water emulsion base carefully balanced proportions of tar, sulphur, and salicylic acid—three of the drugs that are fundamental in dermatological practice.

'Pragmatar' is miscible with serous exudate: it is not gummy, and is easy to apply and to remove. In the general care and hygiene of the seborrhoeic scalp, 'Pragmatar' may be left in the hair as a light dressing.

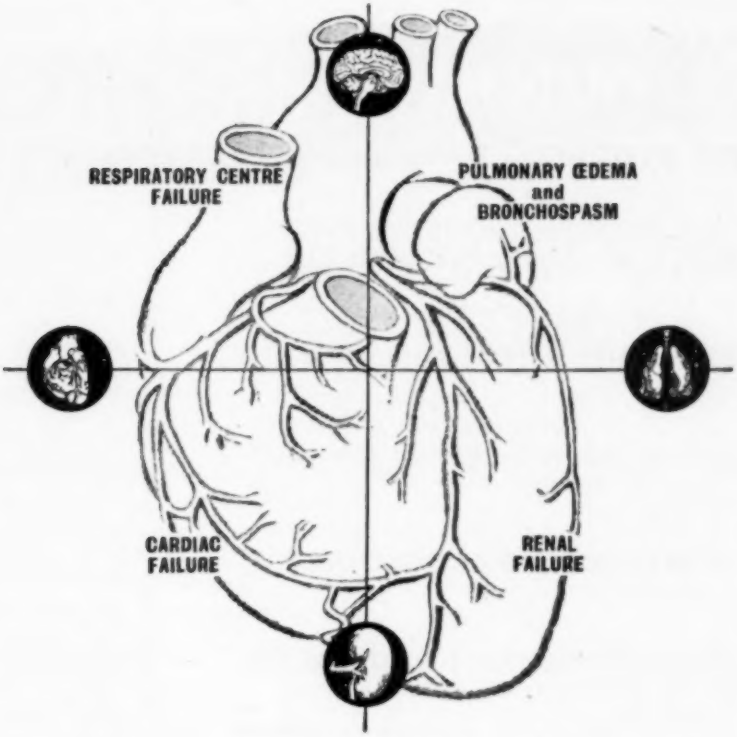
'Pragmatar'

Formula: Cetyl-alcohol-coal-tar-distillate, 4%; Sulphur, 3%; Salicylic acid 3%, in a water-miscible base.

Seborrhoeic Dermatitis
Eczematous Eruptions
Psoriasis
Fungous Infections

Issued in 1-oz. tubes

MENLEY & JAMES, LIMITED, COLDHARBOUR LANE, LONDON, S.E.5
for *Smith Kline & French International Co., owner of the trade mark 'Pragmatar'* PRP23



Cardophylin provides **4** point coverage

in controlling the various complications of heart failure

Benger Laboratories

Cardophylin is presented in tablets, suppositories and ampoules for intramuscular and intravenous administration. Literature is available on request.

Cardophylin— manufactured by Whiffen & Sons Ltd., is distributed by

BENGER LABORATORIES LIMITED • HOLMES CHAPEL • CHESHIRE • ENGLAND

"Aluminium phosphate gel produced prompt relief of ulcer pain, had an excellent effect on appetite and return of strength and was much less constipating than aluminium hydroxide."

Amer. J. Dig. Dis., 1945 **12**, 65.

Aluphos is a non-systemic antacid which cannot cause acid rebound even following overdosage. It is free-flowing and ideally suitable for administration by intra-gastric drip. Further information on request.

Aluphos TRADE MARK

ALUMINIUM PHOSPHATE GEL

A product of Benger Laboratories

BENGER LABORATORIES LIMITED • HOLMES CHAPEL • CHESHIRE • ENGLAND

IN ESSENTIAL HYPERTENSION

A CENTRALLY-ACTING VASORELAXANT WITH A POTENT HYPOTENSIVE ACTION

VERILOID *

An outstanding feature of the hypotensive action of Veriloid is its central action, which effects vaso-relaxation by impulses transmitted to the arteriolar musculature. Ganglionic function is not disturbed, therefore there is no interference with the postural reflexes essential for normal activity.
Veriloid, a unique preparation of the ester alkaloids of Veratrum viride, is specifically indicated in all grades of essential hypertension. Because it is biologically standardized in dogs, its clinical effect is significant and dependable. If dosage is carefully adjusted, control of blood-pressure throughout the whole day is entirely possible.

Veriloid (plain)

Supplied in scored tablets of 1 mg. and 2 mg. Average dose: 9 to 15 mg. divided into three doses at 6 to 8 hourly intervals preferably after meals.

Veriloid-VP

Scored tablets of Veriloid, 2 mg. with Phenobarbitone, 15 mg. Provides mild sedation, and also enables effective hypotensive doses to be given to patients readily nauseated by Veriloid given alone.

Veriloid Intramuscular & Intravenous Solutions

Produce an immediate and pronounced reduction of blood-pressure and find valuable application in the treatment of acute episodes of hypertension, e.g. malignant hypertension, encephalopathy and eclampsia.

* Trade Mark of

RIKER LABORATORIES LIMITED, 29 KIRKEWHITE ST., NOTTINGHAM

A copy of the comprehensive brochure "Veriloid in the Management of the Hypertensive Patient" will gladly be sent to Physicians requesting it

COMBINES THESE 12 IMPORTANT FEATURES

1 Uniformly potent. Its constancy of pharmacological action permits calculation of exact dosage in milligrams . . .

2 A unique process of manufacture produces a tablet which dissolves slowly, assuring absorption and action over a considerable period . . .

3 Moderates blood-pressure by vasorelaxant action independent of vagomotor effect . . .

4 No ganglionic or adrenergic blocking . . .

5 Lability of blood-pressure, so important in meeting the demands of an active life, is not interfered with ; no danger of postural hypotension . . .

6 Cardiac output is not reduced . . .

7 No compromise of renal function .

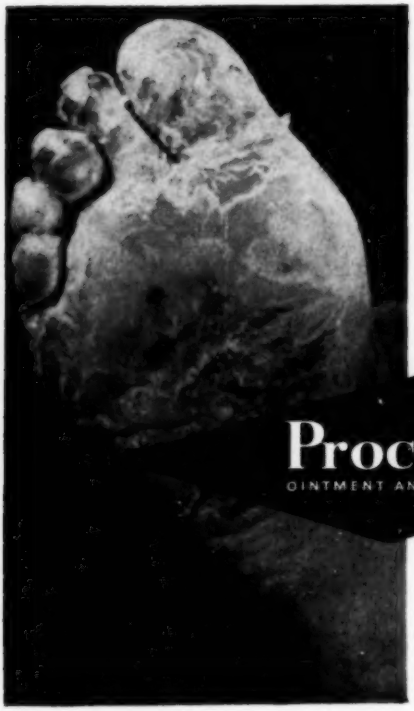
8 Cerebral blood flow is not decreased . . .

9 Tolerance or idiosyncrasy rarely develops . .

10 Hence can be given over long periods with the aim of arresting or lessening progression of hypertension . . .

11 Well tolerated in properly adjusted dosage; does not occasion headache . . .

12 Produces a prompt and sustained reduction of blood-pressure in all forms of hypertension . . .



QUICK EFFECTIVE

treatment of

ATHLETE'S FOOT

in the *chronic stage** can be obtained by the use of

Procelium

OINTMENT AND POWDER

—a Whitfields formula plus undecylenic acid, powerfully keratolytic and fungicidal, in its mixed paraffin and lanolin base.

Applied freely to the sodden mycelium ridden layers of the skin, 'PROCELIUM' will quickly penetrate into the affected area and clear up the condition. 'PROCELIUM' Dusting Powder should be used to prevent recurrence of the infection.

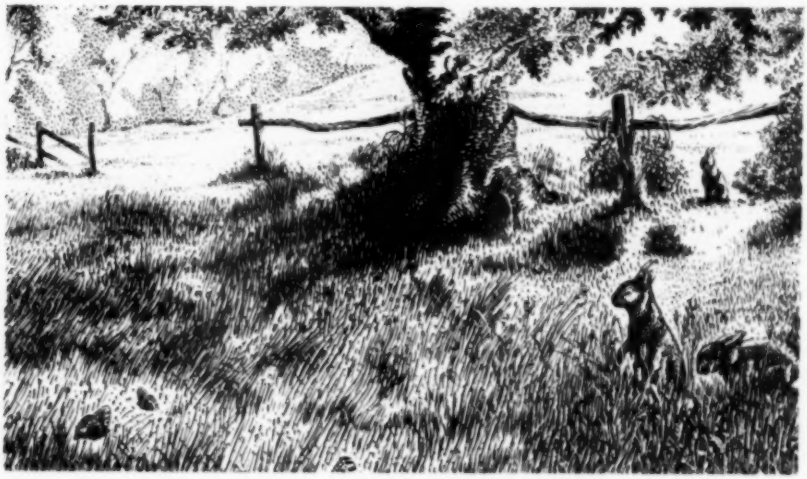
* *In the acute phase of Athlete's Foot this powerful Keratolytic must not be applied. Here the soothing and fungicidal action of 'Zicthol' Green is indicated. Where the acute phase is complicated by eczema of the palms and interdigital clefts this condition should be cleared with 'Zicthol' using 'Zicthol Green' only on the foot.*

Write for further details to 'The Medical Dept.'

GENATOSAN LTD *Loughborough, Leicestershire, England*

"I dread the rustling of the grass"

WILLIAM WORDSWORTH



NO sooner has the blossom languished and spring shed her coat of many colours than the tall grasses ripen. The air is again pollen-laden. To those who love the countryside these richly-clothed meadows are a joy: to sufferers from hay-fever they are merely the signal for a fresh period of acute discomfort. Yet there is a solution—**BENADRYL**, probably the most potent of all histamine antagonists, may be taken just before and during the pollen seasons and, in the majority of cases, provides effective relief.

BENADRYL **a successful anti-histamine**

Capsules (25 or 50 mg) in bottles of 50 and 500
Elixir in bottles of 4 and 16 fl. ozs.

Parke, Davis & Co. Ltd. *Inc. U.S.A.*, Hounslow, Middlesex. Tel.: Hounslow 2361

262

The Relentless Mirror

Time is a gentle deity . . . but how cruel it can be to woman in her middle years

To the woman at the menopause, a glance in the mirror reveals so much more than a reflection of her face. Apprehension, flushing, irritability and depression confront her and the calm philosophy that has stood her in good stead through the years no longer mellows her reflection.

Euvalerol M, the ideal sedative in menopausal conditions, alleviates nervous phenomena and vasomotor disturbances and restores the emotional outlook.

Euvalerol M contains a preparation obtained from valerian root from which the unpleasant odour, characteristic of valerian, is eliminated. To each fluid drachm (4 c.c.) of this odourless preparation of valerian are added ¼-grain (16 mg.) of phenobarbitone and 0.1 mg. of stilboestrol.

EUVALEROL M

In bottles of 4 and 8 fluid ounces.

Literature on application.

ALLEN & HANBURYS LTD LONDON E 2

TELEPHONE BISHOPSGATE 8201 (17 LINES) TELEGRAMS "GRIFFENBURYS BETH LONDON"

In Dysmenorrhoea

BELLERGAL

a sedative of the entire autonomic nervous system, relieves pelvic pain, nausea and depression. Treatment with Bellergal is best commenced 3 days before menstruation with the administration of 1-3 tablets daily. Upon the onset of menstruation, one tablet is given every 2-3 hours, up to a maximum of 6 tablets per day, until relief is obtained. (*Med. Rec.* 1935, **142.** 241.)

Each Bellergal tablet contains: 0.1 mg. Bellafoline, 0.3 mg. ergotamine tartrate B.P. and 0.02 g. phenobarbitone.

Literature and samples available on request

SANDOZ

SANDOZ PRODUCTS LIMITED

134, Wigmore Street, London, W.1.

THE LATEST
INHALATION
ANAESTHETIC

"NEOTHYL"

Brand of
METHYL N-PROPYL ETHER

Clinical trials of methyl n-propyl ether have shown that it is superior to diethyl ether as an inhalation anaesthetic in having the useful properties of the latter in enhanced degree without some of its undesirable features.

The new agent has been used with success in a variety of operations, ranging from dental procedures requiring a few minutes' anaesthesia to a craniotomy for brain tumour lasting three hours and a thorocotomy of six hours' duration for oesophageal resection. Open, semi-open and closed circuit techniques were all used; the last method appears to have been that preferred in the majority of cases.

Samples and literature upon application

J. F. MACFARLAN & CO. LTD.

8 Elstree Way
Boreham Wood, Herts.

109 Abbeyhill
Edinburgh 8

energy and well-being

depressive states

of psychogenic origin

A new pleasantly flavoured tonic and stimulant for the relief of mild depression and lethargy.

Depressive conditions are commonly associated with persistent pain, chronic organic disease, the climacteric, and old age. 'Adetate' relieves the symptoms, giving a feeling of well-being and increased energy. It is also of value as an adjunct in the control of obesity.

Initial dosage should be small, and increased gradually until the desired effect is reached. For adults, 1 to 3 teaspoonfuls daily in divided dosage is suggested, given before meals, the last dose of the day before 4 p.m. to avoid interference with sleep.

'Adetate' Additive Elixir is supplied in bottles of 4 and 16 fluid ounces.

Literature and clinical package gladly sent on request.

Each fluid ounce contains:

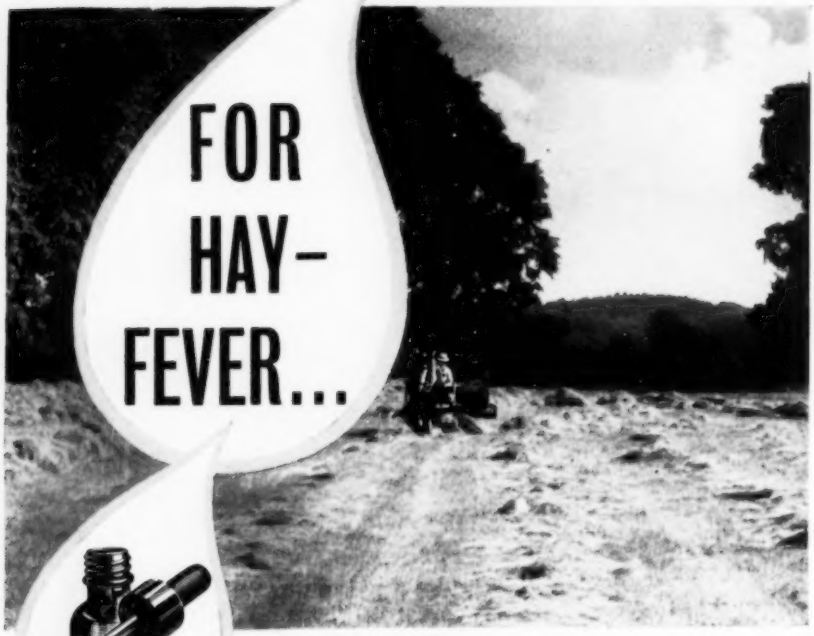
Dexamphetamine sulphate	*30 mg.*
Aneurine (thiamine) hydrochloride	*30 mg.*
Sodium glycerophosphate	*240 mg.*
Potassium glycerophosphate	*60 mg.*

SHARP & DOHME

Elixir **'ADETATE'**
Trade Mark

SHARP & DOHME LTD., HODDESDON, HERTS.

FOR HAY-FEVER...



THE CONTROL of hay-fever still remains a problem, but whatever therapy is adopted the additional use of a nasal decongestant is invaluable.

FENOX, by virtue of its unique properties, is the ideal preparation, providing immediate and prolonged relief without . . .

irritation of inflamed mucosa
impairment of ciliary action
undesirable side-effects

FENOX is water-miscible and non-oily. It has the same viscosity as mucus and remains at the site of action.

FENOX—*Isotonic Nasal Drops of Phenylephrine and Naphazoline*

Supplied in ½ fl. oz. dropper bottles

May be prescribed on Form E.C.10. Basic N.H.S. price 1/8

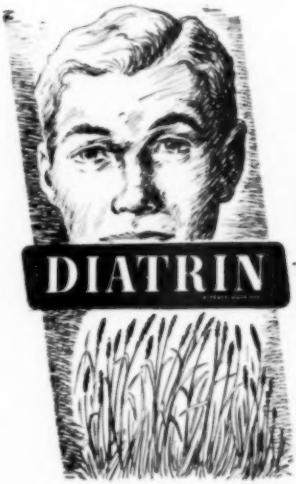
FENOX

NASAL DROPS

BOOTS PURE DRUG COMPANY LIMITED
STATION STREET NOTTINGHAM

Boots

SISSA



Barrier Action

Hay fever, that seasonal scourge, is now coming into its own, but relief can be provided for the allergic sufferer by the antihistamine drugs, which erect a barrier against the action of histamine.

Diatrin* produces just such a barrier, giving reliable protection at this time and rapidly bringing much-sought relief. Diatrin is, moreover, equally active in controlling many other allergic symptoms, its particular value lying in the way it combines low toxicity with marked antihistaminic effect. It is very well tolerated and is remarkably free from side-effects.

Diatrin is presented as a sugar-coated tablet of 50 mg. strength. In most cases one tablet, given four times daily, brings prompt and effective relief.

INDICATIONS Urticaria, chronic and acute (particularly the acute). Hay fever. Allergic vasomotor rhinitis. Atopic eczema and dermatitis. Contact dermatitis. Drug rashes (penicillin, etc.). Neurodermatitis. Pruritus. Erythema multiforme. Vernal conjunctivitis.

FORMULA. *N,N-dimethyl-N'-phenyl-N'-(2-thienylmethyl)-ethylenediamine monohydrochloride.*

PACKING. Diatrin Hydrochloride 'Warner' is available as sugar-coated oral tablets, 50 mg. each—bottles of 20 and 250.

NO WARNER PREPARATION HAS EVER BEEN ADVERTISED TO THE PUBLIC

William R. **WARNER** *and Co. Ltd. Power Road, London W.4.*

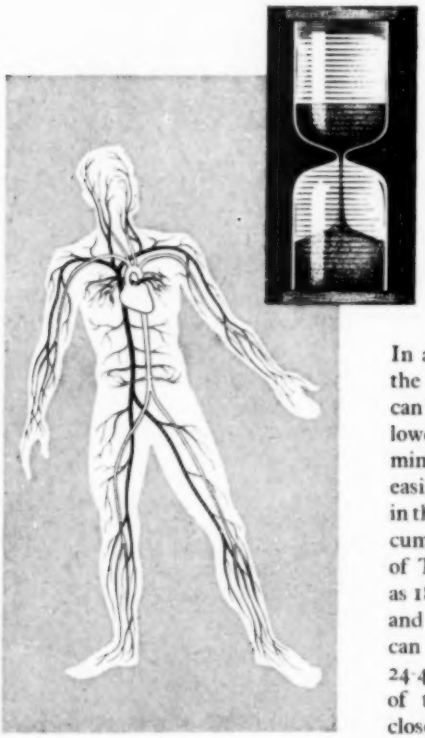
The adolescent is often anxious about his appearance, so that even mild acne appears to him a serious and repelling disfigurement. His anxiety to hide his spots may be so great as to make him hide himself and avoid the society of his fellows.

'Eskamel' *for acne*

'Eskamel' hides his spots for him. It is delicately flesh-tinted so that it is almost invisible when applied, and it often produces such marked improvement that, in a matter of weeks or days, there is nothing to hide.

Resorcinol (2%) and sulphur (8%) in a stable, grease-free, flesh-tinted base. Issued in specially lined 1-oz. tubes.

MENLEY & JAMES, LIMITED, COLDHARBOUR LANE, LONDON, S.E.5
EMP53 for *Smith Kline & French International Co., owner of the trade mark 'Eskamel'*



when time is vital...

In any thrombo-embolic emergency, the oral administration of Tromexan can be relied upon to produce a prompt lowering of the prothrombin level with minimum risk. It is readily soluble, easily absorbed, absolutely non-toxic in therapeutic dosage and only slightly cumulative. While the maximal effect of Tromexan is exhibited in as little as 18 to 24 hours, elimination is rapid and a normal prothrombin level can usually be re-established within 24-48 hours by the simple cessation of treatment. Thus a remarkably close measure of control is assured*.

TROMEXAN

Geigy

Bis - 3, 3' - (4 - oxycoumarinyl) - ethyl acetate (B.O.E.A.)

. . . for greater safety and control in anti - coagulant therapy

In tablets of 300 mg. and 50 mg. each.

Literature on request.

* *For routine prothrombin estimations, standardised THROMBOKINASE GEIGY is available in convenient, stable, time-saving tablets—closed tubes of 10 x 10 mg. tablets.*

PHARMACEUTICAL LABORATORIES GEIGY LTD

Rhodes, Middleton, MANCHESTER

PH.41c

An Effective Analgesic

WHILE modern chemical research has evolved many and diverse analgesics, the popularity of acetylsalicylic acid and its reputation for effectiveness remain. Nevertheless, some physicians have hesitated to employ it owing to its tendency in certain conditions, to irritate the stomach.

In 'Alasil', however, the desirable therapeutic effects of acetylsalicylic acid are maintained without the tendency to irritation by combining the acid with 'Alocol' (Colloidal Aluminium Hydroxide), an effective gastric sedative and antacid. Thus 'Alasil' helps to solve the problem of administering acetylsalicylic acid in an effective form, even to patients with sensitive stomachs.

The advantages of 'Alasil' have been well proved in practice. Experience shows that it can be prescribed with safety to patients of all ages.

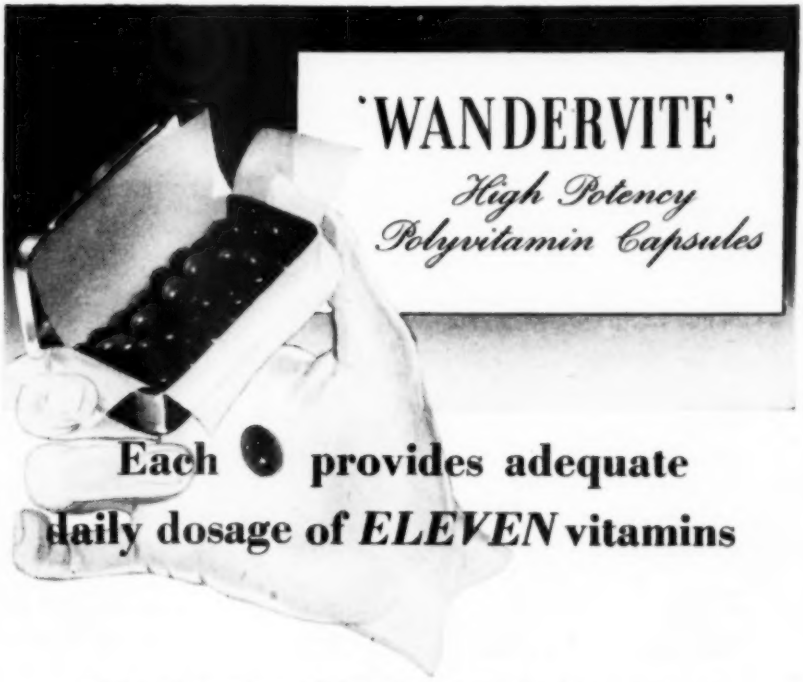
Alasil

A supply for clinical trial with full descriptive literature sent on request.

A. WANDER LIMITED
42 Upper Grosvenor St.,
Grosvenor Square,
London W.1

As 'Alasil' is a purely ethical product and not advertised to the public, it can be prescribed under the N.H.S. on Form E.C.10

M322



'WANDERVITE'

High Potency Polyvitamin Capsules

Each ● provides adequate daily dosage of *ELEVEN* vitamins

EACH 'WANDERVITE' CAPSULE provides the approximate adult daily requirement of each of its eleven constituent vitamins.

FORMULA (each capsule)—

Vitamin A ..... 5,000 i.u.	Vitamin B_1 ..... 2.5 mg.	Nicotinamide ..... 15 mg.
Vitamin C ..... 50 mg.	Vitamin B_2 ..... 2.5 mg.	*d*-Calcium pantothenate ... 5 mg.
Vitamin D ..... 1,000 i.u.	Vitamin B_6 ..... 1 mg.	Folic acid ..... 0.1 mg.
Vitamin E ..... 5 mg.	Vitamin B_{12} ..... 1 μg.	

Because a diagnosis of deficiency of one vitamin or group often implies shortage of other vitamins, treatment of vitamin deficiencies requires a balanced supply of the important accessory factors whose presence is known or believed to be essential to normal health. 'Wandervite' Capsules provide this.

ADVANTAGES—

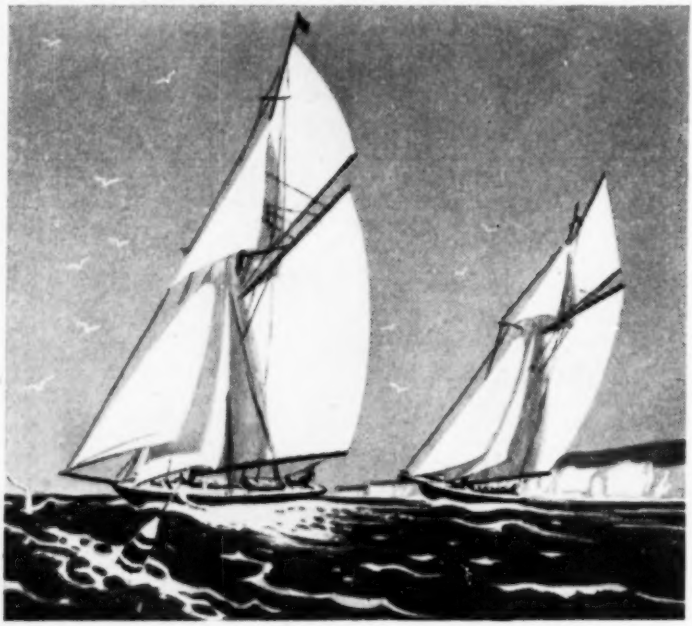
Economy **Comprehensiveness** **Convenience of shape and size**
Adequate daily dosage in each capsule

PACK: Tin of 30 Capsules (1 month's supply)

Strictly ethical

M.185

A. WANDER LTD., 42 Upper Grosvenor Street London W.1. Phone: GROsvenor 3931 (10 lines)



Free to breathe again

Most cases of asthma respond excellently to 'Neo-Epinine'. More effective than adrenaline or ephedrine as a bronchodilator, it has the further advantage that it is relatively free from side-effects. Rapid relief follows the use of 'Neo-Epinine' No. 1 Spray Solution, a plain 1 per cent aqueous preparation. 'Neo-Epinine' sublingual products, 20 mgm., act within 5-10 minutes. Stubborn cases may need 'Neo-Epinine' No. 2 Compound Spray Solution, which contains 1 per cent of the drug with 2 per cent of papaverine and 0·2 per cent of atropine methonitrate.

'NEO-EPININE'
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THE PRACTITIONER

No. 1019 MAY 1953 Volume 170

THE MONTH

The Symposium

Some of the most spectacular advances in medicine of recent years have taken place in ophthalmology. In addition, this, one of the oldest specialties in medicine, has benefited from the general advances which have characterized the last decade. It is these aspects of the subject which have been selected for consideration in the symposium this month. Acrylic lenses and successful corneal grafting are the culmination of many years' patient research, and their present status is reviewed by Mr. A. J. B. Goldsmith and Mr. McKie Reid respectively. The rapid advances in chemotherapy and the discovery of the therapeutic rôles of cortisone and ACTH have had profound repercussions upon the treatment of diseases of the eye, as is well brought out by Professor Arnold Sorsby in his article on 'specific treatment of ocular infection', and by Professor W. J. B. Riddell in his article on 'cortisone and ACTH in ophthalmology'. On the debit side is the unwelcome intrusion into this field of retrolental fibroplasia as a cause of blindness in children, a subject which is reviewed by Mr. J. H. Doggart. Finally, there is the ever-recurring problem of toxic amblyopia, which is discussed by Mr. G. I. Scott. Many of the procedures outlined in this symposium are obviously beyond the scope of general practice, but we feel that the man in practice will appreciate this expert guidance to what can now be accomplished by the specialist to whom he refers his patients with ocular disturbances.

The Queen and the College

For the past year those whose journeys take them through Lincoln's Inn Fields will have noticed signs of activity in the bombed areas to the east and south of the College of Surgeons, where in 1941 the world's greatest surgical museum was laid waste by an air raid and the fire that followed it. The site has been cleared of debris, the foundations of the intended structure have been laid, and within the last few months a steel skeleton has risen above the hoardings. On May 5, the memorial stone which marks the official inception of the new building will be laid by her Majesty the Queen. To celebrate the occasion we are publishing in this number (p. 488) an article on the College, and its Royal associations, by Sir Arthur MacNalty who has done so much to make the profession familiar with the history of the College.

These new premises will be a tribute to the vision and enterprise of Alfred Webb-Johnson, one of the great Presidents in the history of the College. They mark the beginning of a new era in its history rather than a

restoration of its former glories. They will represent in brick and stone the new rôle of the College as a centre of surgical research, as a postgraduate school where students from every land may learn the tenets and practice of British surgery and study the basic sciences on which it is founded, as a home for the associations representing surgical and allied specialties, and as a meeting place where any surgeon passing through London will find welcome, entertainment and fellowship. In the new buildings will be a residential college to house visiting postgraduates, established and endowed by the munificence of Lord Nuffield. There will be museum space for the three new chairs of Anatomy, Physiology and Pathology. There will be added library accommodation, several more lecture theatres, and offices for all the Faculties. These departments will be grouped round a great hall in which public lectures and public banquets can be held. When an Academy of Medicine takes shape, as it eventually must, these public rooms will be ready to form a nucleus for a union and regrouping of the Colleges representing the main branches of medicine, of which not the least will be the College of General Practitioners.

Reason at Last

From its inception the National Health Service has been subject to two fundamental handicaps. The first was the precipitate manner in which it was foisted on the country without any knowledge of what was involved. The second was the absence of any clear long-term plan of development. When the Treasury, not unnaturally, became alarmed at the apparently endless demands which the Service was making upon the national income, all that successive Ministers of Health could apparently do to try and keep within the financial limits imposed upon them was to place artificial 'ceilings' on annual expenditure in different sections of the Service, irrespective of the over-all development of a coordinated and rational Service. Such short-term measures did more harm than good in that, by and large, they failed to achieve their financial aims and at the same time caused needless frustration and dissatisfaction among all departments of the Service.

Since assuming office, the present Minister of Health has shown a refreshingly sympathetic and intelligent understanding of the many problems which he inherited from his predecessors, and in all his announcements has made it abundantly clear that his aim is to provide the country with the best possible National Health Service which the country can afford. His latest move is the logical sequel to the policy which he has consistently followed: namely, the setting up of an independent committee, under the chairmanship of a distinguished economist, 'to review the present and prospective cost of the National Health Service' and 'to suggest means . . . of ensuring the most effective control of such Exchequer funds as may be made available'. At long last there are grounds for believing that it will be possible to evolve a long-term policy for the Service based upon facts—

rather than political fancies. The new committee has not an easy task in front of it, but it can be assured of the wholehearted support of all who are determined that the country shall have a Health Service which will be an amalgam of all that is best in private and public enterprise.

'The Delicate Child'

In our persistent emphasis upon the prevention of disease and its early recognition there is a very real danger, unless considerable care is exercised, that we may do as much harm as good. In striving to attain an ideal standard of health we may inadvertently prevent a not inconsiderable proportion of the nation from living as full lives as they might have done. An important aspect of this problem is well brought out in the annual report, for 1951, of the School Medical Officer of the County Council of the West Riding of Yorkshire. In reviewing the work of the year the pædiatrician to the Council comments: 'If we consider the wastage of school time between 7 and 11, which is educationally irremediable, we need to review the fallacy that "health is more important than success". Scores of children are kept off school months at a stretch, instead of days, with "bronchitis" . . . In nearly all such cases, lengthy absence contributes nothing to health, while precluding scholastic success . . . We need to establish that normal people are entitled to certain normal pains'. He quotes two instances of the type of case he has in mind. One was a twelve-year old boy with postural pain due to 'crouching permanently over a television set procured to keep his (innocent) heart murmur away from football fields'. The other was a grammar-school girl who lost five weeks from school because of 'a dizzy sinking feeling on rising, which amounted to healthy hunger contractions'. Incidentally, it is of interest to note that his records of innocent heart murmurs still outnumber the rheumatic hearts. Part of the trouble he attributes to the profession: 'By the hesitancy and caution of our pronouncements, by our emphasising the wrong aspect of a situation, or by the failure of inadequate treatment, we easily confirm parents' fears'. On the other hand, 'we wage a defensive struggle against the scorn of dogmatic parents, loth to lose the glamour of abnormality and disease which they have cast over their children'. This is no new problem to the school medical officer, but it would appear to be one that is assuming increasing importance and one which, unless a solution is found, may well have an adverse effect on the future health of the nation.

Adolescent Addicts

We sometimes wonder whether the student of social history realizes what a wealth of information concerning social conditions is to be found within the pages of medical journals. A case in point is a recent article entitled 'Epidemic of narcotic use among school children in New York City' (*J. Pediat.*, 1953, **42**, 65). According to the author, Dr. Harold Jacobziner, of the Department of Health, Bureau of School Health, of New York City, between September 1950 and

February 1952, 167 'verified narcotic (heroin) users were referred for treatment by the School Health Service' of that city. This represents an over-all city-wide rate for the entire school population of 1.53 per cent. According to Dr. Jacobziner, this figure 'probably represents about one-fourth of the total number of narcotic users in the school population'. Of the 167 cases in this particular series, the largest number at any one age was 50 in the 16-year-old group; twelve were fourteen years old and there were ten under the age of fourteen. The majority of these young addicts started off with marijuana cigarettes 'but soon abandoned them and resorted to heroin, "sniffing" or "snorting" (nasal route), "skin popping" (subcutaneous injections), and eventually "mainlining" (intravenous injections)'. The story, told in his own words, of one of these 14-year-old addicts conveys the full tragedy of these unfortunate youngsters: 'A friend gave me a reefer marijuana cigarette in school in May, 1949. Continued smoking marijuana cigarettes for about six months, three to four times weekly, depending on finances. My friend told me that was kid stuff. Before Christmas tried heroin because all my friends were using it. Used it mainly on week ends or holidays. First "snorted" it for several months, then began "skin popping". After a while I used the "mainline" '. Apparently he injected himself in parks, hallways, or on roofs, and was spending as much as $6 a day on drugs. The friend who introduced him to the drug died of an overdose.

It would require the pen of an Emile Zola or a Charles Dickens to do justice to the social background against which tragedies such as these are enacted, but to those with the imagination and experience to read between the lines, this objective, concise medical report will not be lacking in drama. As a picture of the dire effects of the social maelstrom which harries and harasses modern society it deserves the careful consideration of all who are concerned with the welfare of the youngsters of today.

Coronation Number

As the symposium for our June number, fuller details of which will be found on p. lxx, we have selected an aspect of general practice which has never received the serious and detailed consideration which it merited, namely its organization. The doctor's house, his surgery, his waiting room, his filing and indexing system, his income-tax and accountancy problems, his car—these are all vitally important aspects of his work which are largely ignored in his training, and once he is embarked upon practice he seldom has the time to compare notes with his colleagues, or the opportunity to discuss the relevant problems with the appropriate experts. In our symposium, which is largely written by general practitioners, with the assistance of architects, accountants and motoring experts, we hope to be able to provide the man in practice with practical suggestions for improving the conditions under which he works.

SPECIFIC TREATMENT OF OCULAR INFECTIONS

By ARNOLD SORSBY, M.D., F.R.C.S.
Research Professor of Ophthalmology, Royal College of Surgeons, and Royal Eye Hospital.

'Merely to increase the contents of our pharmacopœia is not to add to our resources . . . I have endeavoured . . . to give pharmacology an ætiologically therapeutic tendency' (Paul Ehrlich: 'Experimental Researches on Specific Therapeutics', The Harben Lectures for 1907).

It is now nearly twenty years since an incredulous world heard of prontosil rubrum as an agent against streptococcal infection. There was disbelief, for had not intensive chemotherapeutic work over the better part of a quarter of a century left N.A.B. as almost the sole achievement in that field? Chemotherapy had come to be regarded not as the logical outcome of Ehrlich's work, but as a rather unwarranted and grandiose name for an empirically discovered arsenic preparation. In this mental climate specific therapy in Ehrlich's sense was hardly a feasible objective.

Today chemotherapy is still an unfulfilled objective. Control in infectious diseases has been achieved by the developments inspired by chemotherapy rather than by chemotherapy itself, for if the sulphonamides are chemical agents, penicillin and the other antibiotics—which together have a far wider range than the sulphonamides—are largely a by-product of bacteriology. Specific therapy has been achieved to a considerable extent, but not in the chemical sense visualized by its pioneers, and the problem today is no longer the feasibility of treating infections specifically or non-specifically, but of using available resources to achieve therapeutic results quickly and effectively. This is often, but not always, possible, for the immense achievements during the last twenty years must not blind one to the fact that an important group of infectious diseases is still beyond adequate control. The rickettsias and larger-sized viruses show some response to the newer antibiotics, but virus disease as a whole still remains an unsolved problem.

Specific therapy implies specific diagnosis, differentiating the lesions due to organisms susceptible to sulphonamides or antibiotics from lesions due to organisms without such susceptibility; it goes further, for it seeks to differentiate the lesions caused by susceptible organisms, so that a particular sulphonamide or antibiotic can be used as the most effective for the infection in question. A sloughing corneal ulcer may be taken as an illustration: it is essential to recognize by clinical or laboratory means whether the infection is caused by a gram-positive organism susceptible to penicillin, or a gram-negative organism which would respond only to streptomycin, or possibly by a virus which responds to neither.

Since specific therapy is impossible without accurate diagnosis, differential diagnosis must sort out the different types of infection from each other. At the very least it must seek to distinguish infection from a non-infective

inflammatory reaction, for here there is no specific therapy, and indeed no treatment by sulphonamides or antibiotics.

SPECIFIC DIAGNOSIS

Purulent and muco-purulent conjunctivitis

A red eye is not evidence of infection. The eye may be congested from an attack of acute or subacute glaucoma, or of acute iritis. Glaucoma is definitely not an infective lesion, and very few cases of iritis are infective in origin—iritis is usually an inflammatory reaction from unknown causes. Definite evidence of infection is presented by a purulent, or muco-purulent, discharge from the conjunctiva. In the absence of such discharge the presumption is in favour of an inflammatory reaction rather than infection, except that infection with non-pyogenic viruses produces a conjunctival reaction largely indistinguishable from inflammation. Purulent conjunctivitis, typically seen in ophthalmia neonatorum, may be caused by many different organisms. An accurate bacteriological examination is generally of no great importance, as most pyogenic organisms are sensitive to both penicillin and sulphonamide. If, however, within twenty-four hours of instituting adequate penicillin or sulphonamide therapy the infection is not well under control, one may safely assume that it is due either to gram-negative bacilli, or to the rare cases of insensitive strains of organisms normally sensitive to the sulphonamides and penicillin.

Infections of the cornea

Differential diagnosis in corneal lesions is particularly difficult. Many corneal lesions are inflammatory rather than infective: some of the inflammatory reactions may be due to infection by non-pyogenic viruses; some, as phlyctenular ophthalmia and interstitial keratitis, are allergic or anaphylactic in type; some, like the corneal dystrophies with their distinct mode of inheritance, are genetically determined. Of the frank infections of the cornea, by far the most common is the group of serpiginous ulcer with greyish, obviously infected margins and hypopyon; the pneumococcus is a frequent, though by no means the commonest, infecting organism, staphylococcus and streptococcus being responsible for the majority of cases. These are penicillin-sensitive organisms, and response to modern treatment is excellent—a striking contrast to the poor results obtained in the past.

Occasionally an infected corneal ulcer is caused by gram-negative bacilli. The clinical picture is generally characteristic. Instead of an infected serpiginous margin, there is a sloughy, heaped-up base, with a good deal of diffuse corneal infiltration—the effect of the proteolytic action of these organisms. Hypopyon is not a striking feature. These cases do particularly badly if inadequately treated, and do not respond to penicillin.

Other external conditions

Acute virus infections of the conjunctiva and cornea.—The virus infections of the conjunctiva and cornea are exemplified by epidemic keratoconjunc-

tivitis and superficial punctate keratitis. Here there is no purulent and muco-purulent reaction, but a watery discharge with considerable discomfort, and enlarged pre-parotid nodes; often there is a history of an acute respiratory affection. These cases are not readily distinguished from inflammatory reactions, except in the acute stage.

'*Chronic conjunctivitis*'.—Chronic inflammatory reactions of the conjunctiva—the conditions passing under the name of 'chronic conjunctivitis'—are a difficult etiological group. Persistent treatment with the sulphonamides and penicillin only aggravates matters, for drug irritation is superadded to the inflammatory reaction.

Blepharitis.—Inflamed lid margins, especially when acute, may be due to rubbing of the eyelids or to infection spreading from the conjunctiva. The primary lesion should be established and treated. Most cases, however, are of the primary chronic type.

SPECIFIC THERAPEUTIC AGENTS

The sulphonamides.—The original prontosil rubrum rapidly gave way to sulphanilamide which was recognized as the active principle. Of the thousands of sulphonamides synthesized, few are in clinical use, for most have undesirable toxic properties. The sulphonamides used today have generally a relatively low rate of excretion so that frequency of administration can be reduced; thus, sulphadiazine and sulphadimidine are given at six-hourly intervals, and sulphamerazine at eight-hourly intervals. Apart from the many sulphonamides that have been discarded because of their relative toxicity, a clearer appreciation of the value of sulphonamides locally has been achieved. The sulphonamides locally become inactivated in the presence of pus and breakdown products of tissues. Though even now used widely, local sulphonamide preparations, such as sodium sulphacetamide or its proprietary form albucid, are almost entirely useless except for trachoma uncomplicated by local sepsis. Generally speaking, the sulphonamides are effective over a limited range of gram-positive cocci, but the gonococcus—a gram-negative organism—is readily affected. The action of sulphonamides on bacilli is strictly limited, but the effect on some of the large-sized viruses including the virus of inclusion blenorrhœa and trachoma is marked.

Penicillin.—This has the immense advantage over the sulphonamides in being effective both locally and systemically. It is, moreover, highly soluble and non-toxic. It can therefore be used readily in the form of drops, ointment, and subconjunctival injections in high concentrations. Used locally it is essential that the method of application ensures that the ocular tissue is kept in contact with the antibiotic continuously and not merely momentarily at the time of application.

The range of action of penicillin is considerably wider than that of the sulphonamides. Staphylococci in particular are readily susceptible, whilst they are but slightly affected by sulphonamides. Penicillin is also effective against some bacilli, and against the virus of inclusion blenorrhœa.

Streptomycin.—This is almost as soluble as penicillin, though rather toxic when administered systemically. In drops and ointments there is a distinct tendency to local irritation. In subconjunctival injections it is effective in combating corneal infection due to gram-negative bacilli. The place of streptomycin in tuberculous infection of the eye is distinctly limited.

The newer antibiotics.—Aureomycin, chloramphenicol and terramycin are all highly insoluble substances, and as such cannot be applied locally in the form of drops or subconjunctival injections. Suspensions in ointment form have some value. The use of these agents in ophthalmology is further limited by the fact that administered systemically, penetration into the eye is low. These agents with their alleged effect on viruses appear to have little place in ophthalmology, not only because of the limitations in systemic and local use, but because the presumed virus infections for which these agents might conceivably be useful, do not appear to be susceptible. The one striking exception is that chloramphenicol ointment is effective in epidemic kerato-conjunctivitis.

The newer antibiotics have some place in ophthalmology in that they may occasionally be used as rather unsatisfactory substitutes for penicillin or sulphonamides in infections due to insusceptible strains of organisms generally sensitive to penicillin and sulphonamides.

INFECTIONS OF THE CONJUNCTIVA

The purulent ophthalmias

(1) *Ophthalmia neonatorum.*—Only some 20 per cent. of cases are caused by the gonococcus. A considerably greater proportion is caused by the staphylococcus, and most of the common pyogenic organisms contribute a quota. Some 10 to 20 per cent. of cases are caused by a pyogenic virus, morphologically similar to the virus of trachoma. Fortunately, all the different organisms are sensitive to sulphonamides and to penicillin, though to a variable degree. Maximum dosage is therefore essential if the relatively insensitive organisms are to be caught as well as the more sensitive ones.

There are two alternative methods of treating ophthalmia neonatorum; the easier, though somewhat slower, method is the oral administration of sulphonamides. Treatment with penicillin locally gives incredibly rapid results, but calls for considerably more nursing care. As a routine method, when no special facilities are available, treatment by oral suiphonamides is the method of choice. Whichever method is used meticulous attention to detail is essential.

Preliminary steps common to both methods of treatment.—On admission a swab is taken for smear and culture and the eye is irrigated with half-normal saline at room temperature. A drop of adrenaline, 1:1000, is instilled and a scraping is taken from the palpebral conjunctiva for examination for the presence of inclusion bodies. Eye-drops of atropine sulphate, 1 per cent., are instilled if the cornea is affected. Any pus that may have accumulated is wiped away with moist pledgets of cotton-wool.

Procedure for sulphonamide treatment.—(1) After the preliminary measures a tablet of sulphamerazine or sulphadimidine (0.5 g.) crushed into powder is given by mouth in a teaspoonful of water or milk. Alternatively a stock mixture can be used. (2) Sulphamerazine administration in doses of 0.25 g. is continued every eight hours. If sulphadimidine is used the administration has to be at six-hourly intervals. (3) Local treatment consists of three-hourly irrigation with saline solution during the first day in cases with profuse discharge; as a rule there is no need for further irrigation on the subsequent days. After irrigation medicinal paraffin is instilled as a precaution against the sticking together of the lids. (4) Atropine is instilled three times daily in the presence of corneal haze or ulceration. (5) Sulphonamide administration is continued for forty-eight hours after clinical cure.

With this treatment swelling of the lids generally subsides within 12 hours after admission, purulent discharge disappears within 24 hours.

Procedure with local penicillin therapy.—(1) The preliminary measures are completed by the instillation of a drop of penicillin in a concentration of 10,000 units per ml. into the conjunctival sac. (2) The baby is now placed on the nurse's lap, while another nurse sitting near by instils one drop of penicillin solution, 10,000 units per ml., every minute for 30 minutes. Irrigation is not needed, as pus does not form to any extent; such thin mucoid discharge as is present can be ignored or, if it clings to the lid margin, wiped away with moist pledgets of cotton-wool. (3) At the end of this time there is invariably no pus and generally little or no discharge. The eye, however, is still moist, the lids are still swollen, and the lid margins tend to be sticky. The baby is returned to his cot, and instillation of penicillin drops is continued six times at five-minute intervals, followed by a similar number of instillations at half-hourly, hourly, and two-hourly intervals. This gives a total of 22 hours' treatment. Many cases require no further attention. (4) In some babies the lid margins still tend to remain sticky. It is advisable in such cases to continue with penicillin at two-hourly intervals until the eye is dry, when treatment is carried on for a further 12 hours.

Crystalline penicillin only should be used for making up drops. Impure penicillin is likely to cause irritative reaction.

Exceptionally the response to one or other method is not as good as might be expected. In such cases it is essential to change over from one method to the other, and to be guided by bacteriological tests. Rarely streptomycin may have to be used. In no case should local sulphonamides be used: they are ineffective in checking a purulent infection.

(2) *Purulent conjunctivitis in adults.*—This, too, may be caused by a variety of different organisms. There is no fundamental difference in treatment from that employed for ophthalmia neonatorum except that, should oral sulphonamide be used, full adult doses should of course be given.

Muco-purulent conjunctivitis

These cases generally respond rapidly to modern treatment. It is unnecessary to use sulphonamides systemically, for local penicillin therapy is simple and adequate. Any excessive muco-purulent discharge is washed out from the conjunctival sac with luke-warm water. Penicillin ointment, 1000 units of crystalline penicillin per g., is then instilled two-hourly during the day. Within twenty-four to forty-eight hours the eye should be normal.

Virus conjunctivitis

(a) *Acute virus conjunctivitis.*—Epidemic keratoconjunctivitis is endemic rather than epidemic in this country. As already indicated, there is con-

junctival injection, watery discharge, some photophobia, and often an enlarged pre-parotid node, unilateral if only one eye is affected; a history of an acute respiratory infection is common. If corneal involvement supervenes this takes the form of superficial punctate keratitis, demonstrable on staining with fluorescein and by the increase in symptoms. The non-specific measures, such as the use of silver nitrate, only produce further irritation; there is no response to sulphonamides, penicillin, or aureomycin. Rapid resolution occurs when chloramphenicol ointment, 1 per cent., is instilled two-hourly for three or four days.

(b) *Trachoma.*—Mechanical expression of follicles is still an important part of present-day treatment of trachoma, but all the other agents used in the past are now obsolete. After expression the fornix should be painted with 30 per cent. sodium sulphacetamide daily for a month or so. Sulphacetamide ointment, 6 per cent. in a base consisting of 90 per cent. petroleum jelly and 10 per cent. liquid paraffin, should be used three or four times daily. Fresh cases without marked corneal involvement recover rapidly. Where the cornea is involved eye-drops of atropine sulphate, 1 per cent., may have to be used three times daily to keep the iris dilated. In the case of a patient with secondary infection of the conjunctiva when first seen, full doses of oral sulphonamides for three to four days should be given before undertaking expression of follicles and local therapy.

INFECTIONS OF THE CORNEA

Unless a diagnosis of infection by a gram-negative organism is made on clinical grounds when the patient is first seen, every case should be treated at once on the assumption that it is caused by a penicillin-sensitive organism, but a swab from the conjunctiva for bacteriological examination should always be taken. If after twenty-four hours' penicillin treatment has not produced a marked improvement, and particularly so when the culture shows either no organisms or the presence of gram-negative organisms, the penicillin should be discontinued.

Serpiginous hypopyon ulcer or other corneal infection due to penicillin-sensitive organisms.—It is possible that full doses of sulphonamides orally give good results, but the best results are obtained by subconjunctival injection of penicillin. The procedure is as follows:—

> Any sticky discharge present is washed away by cotton-wool swabs moistened in luke-warm water. Two drops of 4 per cent. cocaine are instilled into the conjunctival sac three times, at intervals of two or three minutes, the eye being kept closed during that time. With the eye adequately cocainized the subconjunctival injection can be easily given. This contains 1,000,000 units of crystalline penicillin dissolved in 10 minims (0.6 ml.) of sterile water and 5 minims (0.3 ml.) of adrenaline, 1:1000. A simple way to obtain this solution is to inject these quantities directly into a bottle containing the crystalline penicillin and shake the solution. The clear solution can then be withdrawn into a syringe fitted with a small needle such as a tuberculin needle, and the injection made subconjunctivally at 4 or 5 mm. from the limbus. It helps if someone else keeps the lids separated while the injection is made.

The use of adrenaline ensures that the penicillin does not diffuse too

readily into the surrounding tissues, and in consequence a high and more persistent intra-ocular concentration is attained. Patients generally tolerate subconjunctival injections well, and there is usually no difficulty in repeating a second or third injection at intervals of twenty-four hours if necessary. However, any but the most severe hypopyon ulcers will have responded well to one injection, so that if the hypopyon has disappeared, or almost disappeared, within twenty-four hours, a second injection is unnecessary. Continued treatment, however, is a matter of some importance. The intra-ocular level of penicillin can be maintained at a therapeutic point by instilling penicillin ointment at intervals of two hours during the day for two or three days longer. The ointment should contain 100,000 units per g., and the best base is of some neutral substance, such as 90 per cent. petroleum jelly and 10 per cent. liquid paraffin. Crystalline penicillin only should be used—incorporated direct into the base and not first dissolved.

Proteolytic corneal ulcer due to gram-negative bacilli.—These cases can be satisfactorily treated by subconjunctival injection of 0.5 g. streptomycin in a manner similar to penicillin injection.

Treatment of cases showing no organisms.—As all cases will have received penicillin subconjunctivally (or streptomycin exceptionally) the response will guide further treatment. If the patient is doing well on penicillin the negative bacteriological report should be ignored. If the response is poor after twenty-four hours, streptomycin should be used, for the gram-negative infections are often not readily demonstrated bacteriologically.

Adjuvant treatment.—All cases require to have eye-drops of atropine sulphate, 1 per cent., instilled three-hourly in the affected eye. Where facilities exist the solvent may carry 1/40 grain (1.5 mg.) of atropine sulphate and 1/8 grain (8 mg.) of cocaine hydrochloride in the 10 minims (0.6 ml.) used for dissolving the penicillin or streptomycin.

BLEPHARITIS

Chronic simple blepharitis is generally due to a low-grade infection by penicillin-sensitive organisms. The treatment is simple and consists of removing such scales or scabs as are present by cotton-wool swabs moistened with either hydrogen peroxide 10 vols., or with alkaline solution containing 4 grains (0.25 g.) sodium bicarbonate to the ounce (28.5 ml.). When the lid margins are quite clean, penicillin ointment containing 1000 units of crystalline penicillin per g. should be applied (the ointment base being, as already indicated, 90 per cent. petroleum jelly and 10 per cent. liquid paraffin; and the penicillin directly incorporated in the base in crystalline form, and not in solution). This procedure should be repeated nightly for a fortnight or so. Most cases will respond well. An alternative and older method is to apply paint of brilliant green and crystal violet, B.P.C., instead of penicillin ointment, to the lid margin. This method may be used when penicillin treatment has failed. Chronic blepharitis, however, is often due to poor nutrition, so that relapses are not uncommon unless general measures are also undertaken.

CORTISONE AND ACTH IN OPHTHALMOLOGY

By W. J. B. RIDDELL, M.D., F.R.F.P.S., F.R.S.E.
Professor of Ophthalmology, University of Glasgow.

FOR over a century the structures of the eye have proved to be well suited for the study of inflammatory processes and for the assessment of therapeutic agents of many kinds. The dramatic results reported by Hench and his colleagues at the Mayo Clinic four years ago aroused the greatest interest among ophthalmologists anxious to use these substances for the relief of intractable eye conditions. In this country formal clinical trials have been correlated by a Medical Research Council Panel on the Ophthalmological Application of Cortisone and ACTH, under the chairmanship of Sir Stewart Duke-Elder. This article is derived from the accounts published by the Panel and also the contributions presented to the Ophthalmological Society of the United Kingdom at its meeting last year. The reports of individual observers and of particularly striking cases are appearing in the literature of the world at an increasing rate.

ACTION OF CORTISONE AND ACTH

The collagen, allergic and lymphatic diseases are those in which the steroid hormones have the most dramatic effect. Cortisone is 17-hydroxy-11-dehydro-corticosterone. The parent steroid nucleus is one of the C-11 oxygenated steroids. If the adrenal cortex is stimulated by giving the subject the pituitary adrenocorticotrophic hormone, ACTH, similar clinical responses are produced. The effect of these substances is so powerful that the ordinary functions of the adrenal may be depressed and certain serious effects may result. Glycosuria may be increased or appear for the first time. Protein metabolism may be altered and nitrogen loss be increased. There may be an upset of the potassium levels with a retention of sodium and water, which may produce increase in the volume of plasma and extracellular tissue fluid.

By the use of these substances the picture of an inflammatory reaction can be altered profoundly. There may be a decrease in capillary permeability with consequent reduction of cellular exudate. Granulation and the ordinary fibroblastic healing response are reduced, as is the formation of new capillaries. This is, in brief, a blocking action and if the treatment is stopped the usual tissue reactions establish themselves. There is no antiseptic or bactericidal effect, and it has been shown by Woods (1952) that the inflammatory evidence of an allergic state may be blocked, but the eye reacts in a hypersensitive manner if exposed to the antigen after withdrawing the blocking agent.

Cortisone provides a shield while the disease process burns itself out, but, as Hench put it, the fire is not put out nor does cortisone act as a carpenter

to repair the damage. It must be appreciated that the action is limited to the blocking of the usual pathological reactions to inflammation and no effect is produced upon established structural changes. It is most important that the practitioner should grasp these facts because so many hopes have been raised among patients and the subsequent disappointments may be bitter. It was early recognized that if fibrous tissue formation were to be inhibited in a tuberculous lesion, the spread of the infection within the tissues might be increased.

The action of cortisone on the tissue reactions of inflammation and repair, with special reference to the eye, was the subject of a technical review article by Duke-Elder and Ashton (1951). They came to certain tentative conclusions with regard to the action of cortisone. It has no effect upon the permeability of normal capillaries but the increased permeability characteristic of inflammation is lessened. The exudative phenomena associated with inflammation and granulation tissue formation are both inhibited. The fibroblastic activity observed in tissue repair is diminished with a consequent retardation in the healing of wounds. This effect is particularly evident in the healing of the avascular cornea. A further effect which is well shown in the cornea is the diminution of new blood vessel formation which usually follows inflammation. The precise mechanism of any of these actions is not clearly understood. The fact that subconjunctival injection of a relatively insoluble substance is effective suggests that the hormone acts through some soluble intermediate product.

DOSAGE AND METHOD OF ADMINISTRATION

This summary of the dosage and method of administration is derived from Woods (1952) who has had a wide experience in the use of both ACTH and cortisone at the Wilmer Institute in Baltimore. In order to produce any effect, ACTH must be given systemically as it acts by stimulating the adrenal cortex. When given intramuscularly the initial dose he used was about 20 mg. every six hours, or 120 mg. daily. Thereafter the amount was adjusted according to the therapeutic response and the eosinophil count. If these were satisfactory the amount was reduced by 20 mg. daily to a daily maintenance dose of 20 mg. This might be continued for weeks or months without untoward effect. If the therapeutic response or fall in the eosinophil count was unsatisfactory the amount was increased, in some cases to as much as 240 mg. a day. When given intravenously the effect of ACTH is increased about eight to twelve times. It is given in a glucose drip over an eight-hour period once daily. The usual initial intravenous dose was about 20 mg.

Cortisone may be given by parenteral injection, orally, or by local application. When given parenterally the initial dose was 300 mg. in two divided doses on the first day, 200 mg. on the second and 100 mg. thereafter for a week or a fortnight. It was then slowly reduced. When given orally the amounts were about the same, but divided into four-hourly doses. At the

conclusion of the course ACTH was sometimes given for a few days in order to counteract any depressant effect which the cortisone might have had upon the adrenal cortex. It is sometimes desirable to give 3 g. of potassium daily to compensate for any potassium loss.

Local application to the eye may be carried out by subconjunctival injection, by ointment or by drops; no side-effects are produced and, the eosinophil count being unaffected, the treatment may be used indefinitely. Various observers recommend subconjunctival injection of 5 to 10 mg. about once a fortnight, but the majority of American workers prefer either drops or ointment. The usual saline suspension of cortisone contains 1.5 per cent. benzyl alcohol as a preservative. When used as drops this strength should be diluted 1:4, to avoid irritation. It is instilled every hour during the acute stages of inflammation, and three times a day may be sufficiently frequent as a maintenance dose. The most recent preparation is made up in a buffered phosphate vehicle with 1:5000 zepherin as the preservative and this is almost completely non-irritating, even when used in the full strength of 25 mg. per ml. When used as drops, much of the cortisone may be washed away in the tears and coagulate upon the eyelashes. Woods considers an ointment base to be the best method of topical administration. Cortisone is slightly soluble in mineral oils, so a lanoline or aquaphor base is probably the best. It is used in a concentration of 15 mg./g. every three hours and this is considered to be the effective equivalent of 25 mg./ml. drops used every hour. In external eye diseases and lesions of the anterior segment of the eye, local administration of cortisone is certainly equal, if not superior, to treatment with parenteral ACTH or cortisone. Retrobulbar injections and injection into the anterior chamber following the removal of the aqueous have been carried out, but are not suitable for routine use. Systemic use for eye conditions has to be carried out with care and is contraindicated in patients with diabetes, hypertension, chronic nephritis, and psychotic states.

In acute conditions affecting the anterior segment of the eye cortisone will reduce the reaction to a dramatic extent so long as it is continued. When treatment is stopped the basic condition becomes manifest if it has not expended itself. Thus it is that the classical clinical picture of many lesions may be altered in a dramatic manner, but reverts to the usual state when treatment is stopped. This may have the useful effect of protecting the tissues of the eye from serious or irreversible damage, in the acute phase.

IRITIS AND IRIDOCYCLITIS

In the treatment of acute iridocyclitis cortisone may have a dramatic effect upon the pain, photophobia and lacrimation; within two days the objective signs may clear up and the ciliary injection and exudates in the anterior chamber may have gone. The Medical Research Council Panel reported upon twenty-one patients with a first attack of acute iridocyclitis. In a bilateral case the worse eye only was treated; this rapidly became the better

of the two. Two cases were gonorrheal in origin, four arose from dental sepsis and in the remaining fifteen the etiology was unknown. It was thought that the secondary glaucoma was controlled in several of the patients.

In patients who had had previous attacks the results were similar, but less dramatic. The subacute and chronic groups did not present any marked change in the clinical course. Indeed it was thought that any improvement observed did not last longer than the duration of the therapy. There were six patients of particular interest because the iridocyclitis was associated with rheumatic manifestations. They did not differ in their response from the other patients; the acute cases resolved rapidly, but the subacute and chronic cases did not respond in any dramatic way.

One man had a violent bilateral iridocyclitis of tuberculous origin. There was a small tuberculoma in one eye. Considerable improvement was obtained with streptomycin and PAS during a previous attack. A minute dose of tuberculin was given which gave rise to a violent reaction in both eyes. Six subconjunctival doses of cortisone led to remission within three weeks and the minute amounts of tuberculin were recommended without untoward effect. These were progressively increased and the patient was able to resume his work. In this patient the temporary control of the inflammatory reaction was reported as being of great clinical benefit, and probably allowed the continuation of orthodox treatment without mishap (Duke-Elder *et al.*, 1951).

It would appear that cortisone may be of great value in the treatment of sympathetic ophthalmia and may lead to the retention of eyes with effective vision, which might otherwise have had to be removed. Fortunately, such cases are rare in civilian practice in this country.

CONJUNCTIVITIS

Various types of conjunctivitis have been treated but, taken by and large, the most effective results have been in the cases which were allergic in origin. Spring catarrh may be taken as an example of this and the immediate symptoms of itching and irritation can be greatly relieved. Treatment has to be continued throughout the period of the exacerbation which is a characteristic feature of the disease. The allergic reactions produced by drugs such as atropine and hyoscine have been treated but have not given the uniformly good results in the hands of British workers that have been reported elsewhere. It has to be repeated that the use of this hormone blocks temporarily the signs of acute infective processes and subacute exudative phenomena. By doing so the eye may be protected over a critical period, but the action is limited to the period during which the substance is being used. It cannot be used effectively as a therapeutic agent except perhaps in shortening the duration of a few lesions undergoing spontaneous cure.

CORNEAL ULCERS AND KERATITIS

If the treatment of a corneal ulcer is begun at an early stage before fibrous tissue changes have taken place within the corneal stroma, quite dramatic

results may be obtained. Once infiltrates have appeared and vascularization has begun the results are more doubtful. Recession of the vascularization may give beneficial results, but difficulties of assessment arise. A fundamental difference between the guinea-pig and the rabbit in the action of cortisone on new vessel formation has been reported by Wybar and Campbell (1952). In traumatic ulcers the results seem to be favourable, and in the case of marginal ulcers certain observers report dramatic successes. There is some evidence that delay in epithelial healing may be produced, but it is not thought to be a serious contraindication to cortisone therapy in these cases.

In phlyctenular disease of the cornea and in rosacea keratitis, good results have been published. Care has to be exercised, however, in the assessment of such conditions because of their essentially relapsing nature. Favourable results have not been obtained in the virus infections of the cornea such as superficial punctate keratitis and herpetic lesions.

A somewhat specialized use of cortisone is in the treatment and control of late clouding and vascularization in corneal grafts. It has been suggested that the late clouding is due to an allergic reaction to the donor graft by the recipient and that this can be inhibited by these agents. The treatment should not be instituted for the first two weeks following the operation on account of the possible inhibition of fibrosis (Woods, 1952). It is not known how it comes about that cortisone inhibits fibrosis. It has been shown by Steven (1951) in tissue culture experiments that cortisone had no inhibitory effect in concentrations comparable to those used in therapeutics. He made the stimulating observation that in the presence of living cells cortisone acetate crystals undergo a chemical change by combining with glucose to form a new and soluble compound which may be cortisone-glucoside.

There are reports in the literature of many rare corneal conditions having been treated with cortisone with beneficial results, but such must wait a wider general experience before an opinion can be formed. Disciform keratitis, however, is one in which benefit does seem to be obtained and this is within my own experience. Dramatic effects have also been seen in interstitial keratitis, but this is not a universal finding and I have had disappointing results.

SCLERITIS

The superficial forms of scleritis and episcleritis respond in a dramatic manner to treatment; the more deep-seated have not been so successful. It is thought that this method of treatment is probably better than any other, but the results are not so good as the assumed rheumatic origin of many of them would lead one to expect. Duke-Elder and his colleagues found the results to be more capricious than the literature would suggest.

LESIONS OF THE POSTERIOR SEGMENT

The treatment of acute choroidal lesions was thought to show an initial favourable response but in the chronic cases no change was observed. There

are reports in the literature that central serous retinal lesions responded favourably but these are extremely difficult to assess. The effects upon conditions such as retinal periphlebitis and in recurrent vitreous hæmorrhage have not been good. This might be expected upon general grounds, as many of these cases are thought to be tuberculous in origin. No effect was produced in any of the retinal or choroidal degenerative conditions such as retinitis pigmentosa.

CONCLUSION

The short time during which cortisone has been available, and the small quantities in which it has been received in this country, raise all the problems of statistical clinical analysis in relation to small numbers. Pooled observations from different clinics and countries do not necessarily solve the inherent conflicts. There seems to be little difference between systemic and local administration in reports from American clinics where suitable quantities have been available. In general, the view seems to be that in lesions of the conjunctiva, cornea, sclera, and anterior segment of the eye, local treatment is adequate, and that in lesions of the posterior segment systemic treatment is the more effective. Local treatment has the great advantage of employing the hormone in such relatively small quantities that the undesirable general effects are unlikely to appear.

Work on experimental animals has shown that the local use of cortisone or the parenteral use of either ACTH or cortisone will suppress the ocular reactions to toxins, irritants or actual bacterial infections. The formation of new blood vessels is reduced and within certain limits fibroblastic activity is modified. The action of both ACTH and cortisone is essentially physiological but the precise mechanism is not clearly understood. They have no antibiotic or chemotherapeutic action upon the cause of inflammation, but they may modify the tissue reactions. Thus it comes about that in acute self-limiting conditions the action seems to be specific, although what is really happening is that the disease process is burning itself out while the hormones mask the tissue reactions to which we are accustomed. Woods stated that ACTH and cortisone were of the greatest use in allergic reactions of the external eye and non-granulomatous conditions of the uveal tract. In the chronic granulomatous lesions the effect was not spectacular and recurrences were frequent after the treatment was stopped. It is probable that the use of either ACTH or cortisone is contraindicated in any form of ocular tuberculosis.

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RETROLENTAL FIBROPLASIA

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DWELLERS in the United States of America suffered a severe shock when they were told two or three years ago that retrolental fibroplasia was responsible for one-third of the blindness afflicting children under school age. Here was a new scourge threatening to replace ophthalmia neonatorum and the various other infections which had proved amenable to control by chemotherapy. Consternation was all the greater because many medical men were not yet familiar with the disease. Terry's original but incomplete description did not appear until 1942, and the incidence of retrolental fibroplasia was sporadic. A similar irregularity of distribution was noted in Europe, where, for instance, hardly any cases arose in Switzerland at a time when British ophthalmologists were reporting them in considerable numbers.

NOMENCLATURE

Before proceeding to describe the main features of this disease, it should perhaps be recalled that retrolental fibroplasia literally means the presence of abnormal connective tissue behind the lens. Such tissue often emerges as a developmental defect, and may be accompanied by other signs of ocular malformation. Then again, metastatic endophthalmitis, complicating some febrile illness of infancy, may leave in its trail a mass of organized exudate in the vitreous chamber. Both of these groups might well be embraced by the term 'retrolental fibroplasia' if that expression be literally interpreted, but it is proposed to comply with current clinical usage, so that this article will deal only with that form of retrolental fibroplasia which is alternatively called 'retinopathy of the prematurely born'.

ETIOLOGY

Amidst all the evidence that has been adduced concerning the etiology of retrolental fibroplasia, one factor stands paramount. The incidence is inversely proportional to the birth weight. Statistics show that approximately one in seven of those born weighing less than three pounds (1.4 kg.) are attacked, whereas the figure for babies under four-and-a-half pounds (2 kg.) is only about one in sixteen. Although there have been exceptional cases among full-term babies, it can be assumed for practical purposes that a birth weight of over five pounds (2.3 kg.) will confer immunity.

Although records and case histories have been carefully sifted in various centres, no other factor has been convincingly identified. Owens and Owens (1949) claimed to have prevented the disease by the administration of vitamin E to a group of premature infants. According to these observers,

retrolental fibroplasia attacked several members of a control group comparable in birth weight. Other workers have been unable to repeat these happy results. Thus Bembridge *et al.* (1952) reported retrolental fibroplasia developing in five infants to whom vitamin E had been administered by the method and with the dosage recommended by Owens and Owens.

Oxygen has been drawn into the discussion on two counts. Some have blamed lack of oxygen, and have stated that the incidence of retrolental fibroplasia can be reduced by a plentiful concentration of oxygen in the incubation chamber. Others have produced figures to suggest that high artificial concentrations of oxygen have precipitated the disease. More recently it has been contended that the chief danger lies in sudden lowering of the oxygen concentration. The argument runs that babies of low birth weight must receive a plentiful supplement of oxygen, but that the concentration must be gradually reduced. Otherwise there will be an added hazard of retrolental fibroplasia.

Attempts have also been made, but so far without success, to identify some infective agent which can inflict the disease on an infant predisposed by low birth weight. Nor is there any known association with toxæmia of pregnancy, or with any other antenatal or postnatal complication of childbirth. Among other possible factors that have been taken into account are race, climatic factors, drugs, maternal age and rhesus group—but none of these can be proved responsible. Moreover the sex incidence is approximately equal.

Intensive research continues, but meanwhile it is consoling to note that fewer cases are now appearing in some of the regions most heavily beset a few years ago. It will be recalled that the ravages of maternal rubella have shown wide variations in different parts of the world, and in the same region at different periods. Similar inconsistency in the manifestation of retrolental fibroplasia suggests that perhaps there is some special organism prone to attack the eyes of prematurely born babies, and that the various strains of this hypothetical organism differ in virulence.

CLINICAL COURSE

At first, retrolental fibroplasia was assumed to be a congenital lesion, because cases could not be diagnosed until they had reached the advanced, cicatricial stage, which will be described in the next section. Subsequent work has shown, however, that infants displaying no abnormal ophthalmoscopic signs for a week or two after birth may go on to develop the disease. Some authorities believe that, even in such cases, the pathological process has already begun, but that clinical signs will remain masked until the age of three to five weeks. The active stage lasts for a few weeks or months, and it would appear that in many instances the intra-ocular changes are reversible. In severe cases the outcome is disastrous, because retinal detachment supervenes, and sight is lost. The disease is always bilateral, although one

eye may be more severely implicated than the other. Secondary glaucoma has often been found as a sequel, and that in its turn may produce distension of the globe (buphthalmia).

PHYSICAL SIGNS

Although it would in some ways be more logical to begin with the early signs, it is well first to consider the clinical appearances in an advanced case. In the advanced or cicatricial stage there may be no active inflammatory signs, and the most obvious feature is a pair of inactive greyish pupils in a baby with a blank stare. Closer scrutiny reveals shallowness or obliteration of the anterior chambers, together with atrophy of the irides. Posterior synechiæ are often present. Not uncommonly, near each limbus a series of dentations consisting of elongated ciliary process continuous with degenerate strands of retina is found. Partial opacity of the lenses and corneæ may be noted, and it is usually possible to identify blood vessels entangled in the retrolental fibrous tissue. Sometimes hæmorrhages are manifest therein. Glaucoma has already been mentioned as a sequel, but its onset is in many cases prevented by atrophy of the ciliary processes, so that phthisis bulbi rather than glaucoma may ultimately present.

Few medical men have the opportunity to gain much experience of early retrolental fibroplasia, because most of the victims are assembled in units specially equipped for premature infants. Another difficulty is that all forms

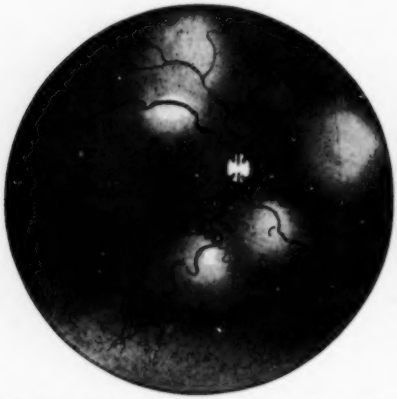

FIG. 1.—Fundus picture of early retrolental fibroplasia in a baby 3½ weeks old. Retinal veins dilated and tortuous. Retinal arteries tortuous. Patches of sub-retinal œdema.

FIG. 2.—The same fundus two weeks later. Sub-retinal œdema has diminished but a vitreous haze has developed over the nasal side of the retina.

of manipulation and examination have to be kept at a minimum when dealing with patients whose life hangs by a thread. Incidentally there are certain fallacies inseparable from the ophthalmoscopy of young babies, if

the observer's previous experience has been limited to older patients. Thus, faint haze of the vitreous may almost be regarded as physiological among infants of low birth weight. Moreover, the average hue of the optic disc is

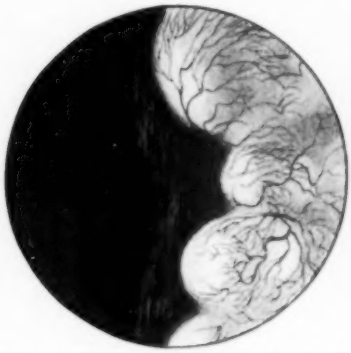

FIG. 3.—The same fundus at the age of 13 weeks. Detachment of retina on nasal side, together with abundant new vessel formation.

FIG. 4.—External view of the same eye at the same stage as fig. 3. Vascularized connective tissue can be seen in the vitreous.

paler in the early months of life than it becomes later. Furthermore, the extreme periphery of the new-born fundus often looks grey and slightly œdematous, so as to simulate an early retinal detachment. Lastly, it must be remembered that physiological macular stippling in early life may be sufficiently conspicuous to deceive the novice into a diagnosis of inflammatory or degenerative change.

In spite of these obstacles to diagnosis, many careful descriptions have been composed, and illustrations prepared, of retrolental fibroplasia in its earliest stages. The first signs consist of retinal hæmorrhage and dilatation of the retinal vessels anywhere in the fundus followed by new vessel formation and œdema of the retinal periphery (fig. 1, 2 and 3). If the changes are limited to hæmorrhages and vascular engorgement, there is hope of complete clearance, followed by the acquisition of normal sight. Œdema and adventitious vessels are of more sinister import, and few cases of complete recovery have been claimed when once these signs have become evident. Fans of newly formed vessels, comparable with those occurring in the retinitis proliferans which is often found in association with diabetes or hyperpiesia, may be seen growing forward from the retina into the vitreous around all or part of the circumference. The more abundant the exudate, the more rapid the onset of detachment, (fig. 3 and 4), and so the retrolental membrane comes to consist of degenerate retinal elements entangled in the products of exudation (fig. 5). Although the active stage seldom lasts for more than ten weeks, changes in the clinical picture may continue to unfold, by reason of ensuing atrophy or glaucoma.

PATHOLOGICAL CHANGES IN AFFECTED EYES

Detailed histological studies have been recorded by a number of authorities, including Reese and Blodi (1951), whose beautifully illustrated article should be studied by those in search of more detailed information. Here it will suffice to point out that the microscope has revealed abundant evidence of inflammation affecting the whole uveal tract. Probably in most cases of retrolental fibroplasia anterior uveitis is secondary to the lesion in the posterior segment, because a similar sequence is often found in adults. It would appear that choroidal exudate attending retinal detachment at any epoch of life can produce an inflammatory response in the iris and ciliary body. The histological slides prepared from eyes irretrievably damaged by retrolental fibroplasia have afforded ample confirmation of the above-mentioned vascular changes, but unfortunately they have not yet supplied an answer to the question whether or not there is an infective agent, and if so, what are its biological characteristics.

FIG. 5.—External view of the same eye from in front at the age of 21 weeks. The development of vitreous fibrous tissue has increased to form a complete retrolental membrane. The other eye was similar in appearance.

ASSOCIATED LESIONS

Reese and Blodi (1951) have more than once drawn attention to the association of skin hæmangiomas with retrolental fibroplasia. Admittedly, hæmangiomas are more commonly found in premature than in full-term infants, but Reese has found that the victims of retrolental fibroplasia, compared with other babies of low birth weight, exhibit more than their share of these skin lesions. In making comparisons, it must be remembered that about 80 per cent. of angiomas are not visible until a few weeks after birth. Reese points out that these tumours tend to increase for about six months, and then recede by a process analogous to the cicatrization of retrolental fibroplasia.

Krause (1946) considered that retrolental fibroplasia was only one aspect of a general neuro-ectodermal derangement attended by mental defect as well as loss of vision. 'Encephalo-ophthalmic dysplasia' was the title which he suggested for this syndrome, but his views have not found general support. There is undoubtedly a form of bilateral retinal dysplasia linked with multiple abnormalities of other regions, including the brain, but this rare condition is often fatal, and is not demonstrably related to a low birth

weight. Let it here be emphasized that most of the victims of retrolental fibroplasia reveal a fair level of intelligence, when due allowance is made for the handicap of blindness arising early in life.

TREATMENT

Various operations have been tried in the hope of tempering the ravages of retrolental fibroplasia. Incisions have been performed with the object of releasing noxious material, and attempts have been made to stave off secondary glaucoma by means of trephining. Some surgeons have gone so far as to excise the abnormal contents of the vitreous. In the light of up-to-date facts concerning the pathology of retrolental fibroplasia it is not surprising that these heroic measures failed. We now know that the clinical picture in an advanced case indicates severe intra-ocular disorganization. Even if the retrolental mass could be removed entire without creating any further havoc in the process, no substantial improvement in vision would accrue, because the very existence of this organized exudate implies widespread detachment of the retina—a condition which necessarily interferes with sight.

Reports on medical treatment have been conflicting, as might be expected from the fact that retrolental fibroplasia is still a novelty. Nevertheless, it is now generally agreed that no therapy can eradicate the later stages of the disease. There is some difference of opinion about the actual border-line between reversible and irremediable cases, but certainly a favourable outcome cannot be expected when once the retina has displayed gross œdema together with an abundant network of newly formed vessels.

Although the vitamin E treatment first advocated by Owens and Owens (1949) can no longer be accepted as a talisman of immunity, many observers still use vitamin E in the belief that it does some good. Vitamins A, D and K have also been recommended. Brown and Corner (1952) report encouraging results from 'neoferrum' (an iron-containing preparation) administered in daily doses of 1 minim (0.06 ml.), gradually increasing to 5 minims (0.3 ml.) by the age of two months, but more evidence is needed before this method can be proved beneficial.

Reese (1951) was impelled to use ACTH on the ground that premature babies are as a rule scantily endowed with cortical steroids. A full-term baby relies upon these substances being supplied through the maternal blood, but premature birth cuts off that source. Reese hoped that ACTH would stimulate the infant's suprarenal cortex, thereby promoting the formation of necessary steroids. In the absence of these substances a premature infant is more likely to reveal angiomatous proclivity. Experiments have shown that ACTH decreases the permeability of capillaries, reduces cellular exudate in the aqueous and vitreous, and inhibits the formation of new vessels. Thus Reese was inclined to suppose that a close analogy existed between the vascularized intra-ocular connective tissue found in retrolental fibroplasia,

and the angiomatous masses which victims of this disease are apt to show elsewhere in the body. Although Reese's experience with ACTH therapy was at first encouraging, he later (Reese *et al.*, 1952) came to the conclusion that this remedy had no effect upon the progress of the disease. On the other hand, Lamotte *et al.* (1952) consider that ACTH is worthy of a further trial.

Until further evidence is forthcoming concerning the value of ACTH, it has to be remembered that retrolental fibroplasia shows wide variations in severity. Thus, many of the cases in which ACTH has been used with apparent success might well have improved spontaneously. It will be recalled that similar variations have been noted in the amount of damage created by maternal rubella and by toxoplasmosis. Unless some effective method of therapy comes empirically to light, the chances of effective treatment are minimized by our ignorance concerning the etiology of this distressing disease.

PREVENTION

Babies predisposed to retrolental fibroplasia by a birth weight of less than four-and-a-half pounds (2 kg.) should be carefully examined at weekly or fortnightly intervals from the age of a fortnight onwards for several months, in order that the disease, if it should arise, can be diagnosed in its earliest phase. Extra oxygen should be made available, but not in a concentration exceeding 50 per cent. Moreover, such concentration should be gradually lowered before a premature baby is released from the incubator. Although no remedy can yet lay claim to be specific, it is reasonable to suppose that careful attention to the general nutrition and welfare of premature infants will probably reduce their liability to be attacked by retrolental fibroplasia.

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THE TREATMENT OF CATARACT WITH PARTICULAR REFERENCE TO ACRYLIC LENSES

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THE origins of cataract surgery are lost in antiquity, nor is it known by whom, or in what part of the world, it was first recognized that removal or displacement of the opaque lens would bring about the restoration of some useful vision.

COUCHING OPERATIONS

It seems probable that the earliest operations were of the nature of couching, in which the cataractous lens was dislocated from its normal position behind the pupil backwards into the vitreous; this allowed of the formation of a blurred image, not properly in focus, on the retina, and gave the patient just sufficient vision to be reasonably independent. These couching operations were performed by inserting into the anterior chamber a sharp thorn or other instrument, and pressing the lens backwards with it, rupturing the suspensory ligament and displacing the lens into the lower part of the vitreous. Alternatively, the same result can be achieved by forcible external manipulation, as in the delightful story of Tobias and the Angel, or it may occur spontaneously. At the present time the couching operation is done only very rarely, and in elderly patients unfit to withstand even the slight physical strain of a cataract extraction and with a short expectation of life.

Its disadvantage was that the dislocated lens floating about within the eye acted as an irritant and in many cases this, together with the low-grade infection introduced into the eye by the operator's favourite thorn, led in a matter of a year or two to loss of vision, or even of the eye from glaucoma. The improvement in vision was good only by comparison with the pre-existing blindness. Really useful vision from the point of view of fine work or manipulations was not achieved until the next advance—the introduction of spectacles, or at any rate by the use of a convex magnifying lens in front of the eye. It is not known exactly when the optical value of lenses was first appreciated—certainly not, on anything like a large scale, before Roger Bacon's time and from the 13th to the 18th century the best that a patient suffering from cataract could hope for was a satisfactory, although probably temporary, result from a crude operation and an equally crude postoperative optical correction.

EXTRA-CAPSULAR EXTRACTION

In the middle of the 18th century Daviel introduced the operation for re-

moval of the lens, or at any rate the bulk of it, a formidable undertaking in the days of pre-anæsthetic and pre-antiseptic surgery. The eyes which survived this procedure, possibly fewer in proportion than those surviving couching, could be counted on to persist as useful organs of vision more or less indefinitely, so that this operation of cataract extraction must be regarded as a revolutionary technical advance. Its value did not achieve universal recognition until the early days of the 19th century, but since then it has been the standard procedure in these cases, becoming much less formidable with the introduction first of general and later of local anæsthesia, and much safer with the dissemination of the principles of antiseptic surgery. During the 19th century the standard operative procedure was what is now called the extra-capsular extraction, in which, after opening the eye, the anterior lens capsule is incised, the hard lens nucleus is expressed and as much as possible of the soft sticky cortex is washed out of the eye by a stream of normal saline. The equatorial zone of the capsule is left, still attached to the suspensory ligament, and the posterior layer also remains, helping to retain the vitreous body in place. In addition, however, a certain amount of cortex is almost inevitably left behind; this absorbs partially and slowly, and while doing so may set up an irritative iridocyclitis. A further drawback is that a film of posterior lens capsule and soft lens matter persisting behind the pupil usually forms a membrane which has sooner or later to be divided by a second operation of capsulotomy, or needling, before the patient can see.

INTRA-CAPSULAR EXTRACTION

The next technical advance came with the development of what is called the intra-capsular extraction, in which the lens is removed complete within its capsule, leaving neither soft lens matter nor a membrane behind, freeing the patient from the risk of iridocyclitis, avoiding the necessity for a capsulotomy and enabling the patient to begin to use his eye within a short time, a fortnight or so, of the removal of his cataract. With increasing knowledge of the anatomy and physiology of the eye, with the introduction of anæsthesia and asepsis and with improvements in instruments and technique, this operation developed out of, and followed naturally upon, the earlier operation devised and introduced by Daviel in 1748.

DISADVANTAGES OF INTRA- AND EXTRA-CAPSULAR EXTRACTION

The latest development in the field of cataract surgery, which it is the purpose of this article to discuss, came with the operation devised by Harold Ridley and described by him last year (*Lancet*, 1952, **i**, 118), in which an acrylic lens of appropriate strength is inserted into the eye to take the place of the natural lens which has become cataractous and has been removed. Before describing and discussing this latest advance, it may be well to consider the reasons, optical, æsthetic and practical, for dissatisfaction with the results achieved by intra-capsular and extra-capsular extractions, reasons

which may not on first consideration appear obvious, particularly when it is realized how grateful is the vast majority of elderly cataract patients for the restoration of their vision brought about by the standard (one need not yet say the old-fashioned) operations and how well they manage with their thick cataract lenses even to the extent of driving cars with a perfectly good legal, if not moral, standard of safety.

It is well known that if a cataract is removed, and provided that the rest of the eye, especially the cornea, vitreous, retina and optic nerve, is healthy, excellent vision will be obtained by cataract glasses, strong convex lenses worn in spectacle frames. The removal of the natural lens from its normal position behind the pupil and its replacement by a glass lens worn some half an inch in front of the eye, introduces, however, a gross alteration in the optical system, the net result of which is that the retinal image formed in the aphakic (i.e. lensless) eye is some 25 to 30 per cent. larger than it is in the normal eye. As a result of this, patients when first fitted with cataract glasses are somewhat disconcerted to find that everything is rather larger than life. (They are often even more disconcerted by seeing, with magnification, the ravages that time has wrought in faces, their own or others', that they may not have seen clearly for years; but this is another story!) To this, however, they rapidly become accustomed. What they find far more troublesome is the prismatic effect induced by looking even a short distance away from the centre of their thick cataract lenses. It will be remembered that on looking through a prism, objects are apparently displaced towards the apex thereof, and that on looking through the edge of a convex lens, a prismatic as well as the usual converging effect is introduced. The result of this is that if a patient looking through the centre of his cataract glasses is conscious of an object which he estimates to be a certain distance away from his line of vision, and turns his eyes, not his head, to look at it, the object will appear to recede from him and his eyes will have to make an angular excursion which to his proprioceptive faculties will appear to be immoderately large. He describes this by saying that objects appear to swirl away when he looks at them and that he has, to begin with anyway, great difficulty in going up and down stairs unless he bends his head down and looks directly at them. This apparent displacement of objects eccentrically regarded can be obviated to some extent by modifying the shape and curvature of the glasses, but it is more difficult to become inured to than size magnification, and because of it many patients, usually of the psychologically unstable type, refuse to wear cataract glasses except for specific purposes such as reading or watching television and when they are sitting still.

Other trials of these patients, which need perhaps to be rated no higher than inconveniences, are that their judgment of distances, as in pouring out tea, for example, is faulty, a defect which improves with time and disappears if vision is restored to both eyes; that without their glasses, even although maybe they can move about, they are considerably handicapped visually and they must remember where they put their spectacles when they

take them off; and that they have no accommodation. To this last most patients of cataract age are already inured; indeed, the wearing of cataract lenses makes life, if anything, easier for them since to read in reasonable comfort they have only to push their distance glasses a little farther from their eyes down their noses.

One much more serious disadvantage remains to be mentioned, which occurs in uniocular aphakic patients in whom the other eye is still normal. In this group of patients, if a uniocular cataract has been successfully removed, and even if perfect vision is obtainable with the proper correcting lens, the disparity of retinal image size makes it quite impossible for the patients to use both eyes together because of intolerable diplopia, the object seen with the aphakic eye being some 25 per cent. larger than that with the normal. Binocular vision is therefore impossible, and as the majority, perhaps, of uniocular cataracts is the result of trauma and occurs in the younger age-groups of the population, a severe handicap is imposed on the patients, particularly in the performance of skilled and precision work. Short of help from contact lenses, to be mentioned presently, they have to lead their life and do their work with their one remaining normal eye, the injured one giving them no more than an indistinct field of vision on that side and, even so, representing no more than a potentially useful visual organ capable of being called into service in the unfortunate event of disaster overtaking the preferentially used normal eye.

It cannot therefore be argued, in spite of the gratification of the patient and perhaps of the surgeon, that the operation for cataract as commonly practised gives a result in any way ideal from the viewpoint of physiological optics. The image is magnified to a disconcerting degree, the clear field of vision obtainable by excursions of the eye alone behind the glasses is much reduced, it is impossible to use together for binocular vision a normal and an aphakic eye, whilst, to be visually competent, the aphakic patient is almost as dependent upon his glasses as were the three Graeae in the legend of Perseus on the one eye which they shared between them.

ACRYLIC LENSES

It has been known for many years that, to a large extent if not completely, the optical difficulties of the aphakic state can be relieved by the wearing of contact lenses which have proved to be of especial value in cases of uniocular aphakia. These, however, have certain disadvantages and do not represent the ideal solution which should, if possible, involve the restitution of normal optical conditions. This cannot be achieved by the grafting or implantation of a normal lens removed from a cadaver or from an excised eye; such would almost certainly survive but, lacking its normal equatorial attachment to the suspensory ligament, it would assume a more spherical shape than normal, would be optically too powerful and would take up so much room that satisfactory closure of the wound would be difficult and subsequent healing prejudiced. The acrylic lens, however, although it has the same refractive

power as the normal lens, takes up considerably less space and, provided that it remains *in situ* without early or delayed complications, affords the best prospect so far available of restoring normal optical conditions apart from accommodative power which it cannot of course provide.

The *technique* of Ridley's operation need be described only briefly.

The cataractous lens is extracted, usually by the extra-capsular technique; a portion of the anterior lens capsule is torn away with toothed forceps, the lens nucleus is expressed, the remaining soft lens matter is washed out thoroughly—and this is very important—by irrigation with normal saline, and an acrylic lens is inserted into the space between the iris diaphragm in front and the posterior lens capsule behind, the latter preventing it from slipping back into the vitreous. The iris is then carefully stroked back into its normal position, a small peripheral iridectomy is performed, the lens is centred by external manipulation through the cornea and the cataract wound is closed by fine sutures of silk. The acrylic, being smaller in all dimensions than the natural lens, has plenty of room in which to accommodate itself and, having a low specific gravity, is easily kept in place by even the feeble diaphragms formed by the iris and the posterior lens capsule. Indeed, in some cases acrylic lenses have been inserted after intra-capsular extractions in which there is nothing to support them posteriorly but the vitreous face over which there is no membrane and the integrity of which appears to be maintained by surface tension only.

The *postoperative course* is usually reasonably smooth but convalescence is slightly more prolonged than after a straightforward intra-capsular extraction. Atropine drops are avoided since, if the pupil is dilated there is some fear of the acrylic lens slipping forwards into the anterior chamber. Postoperative complications are slightly more frequent, the chief ones being prolapse of the iris, treatment of which may entail removal of the acrylic lens, and the deposition of uveal pigment on the front surface of the lens with or without the formation of posterior synechiæ. The latter complications, however, can usually be controlled by the use of cortisone drops started a few days after the operation. If soft lens matter is left behind, and particularly if it is adherent to the posterior lens capsule, it may prejudice the eventual visual result by forming a thin, but optically devastating, layer behind the lens, the removal of which entails a further difficult and complicated operation of posterior needling. The performance of an intracapsular extraction would, of course, obviate this last complication, but most operators are apprehensive of inserting the acrylic lens without some support firmer than that given by the molecular arrangement of the anterior vitreous face, fearing that it might only too easily be spontaneously couched into the vitreous, an occurrence which would necessitate what the operation has been done to avoid, the wearing of cataract lenses, and which might lead to further and more serious complications.

SELECTION OF PATIENTS

In the selection of patients, therefore, it is important to choose only those in whom there is a reasonable certainty of being able to remove all the soft lens matter by irrigation after expression of the nucleus, that is if the acrylic lens insertion is to be done as a primary procedure at the time of cataract extraction. This excludes a large proportion of patients—those with im-

mature cataracts in whom large amounts of soft sticky cortex are present; these cases are best subjected to intra-capsular extraction. If an extra-capsular extraction is done with the idea of implanting an acrylic lens later as a secondary procedure, there is the risk of postoperative iritis with the formation of posterior synechiæ which might well make a later insertion impracticable. Most operators would also regard a history of previous attacks of iritis, or the presence of a flabby atonic iris, as contraindications to performing this type of extraction, whilst in traumatic cases, particularly those in which the cataract has developed as the result of a perforating wound, the possibility of vitreous prolapse at the time of operation has to be taken into careful consideration.

In all, therefore, considerably less than one-half of all patients seen with cataract may be deemed suitable for the insertion of acrylic lenses unless one is prepared to condemn them to long periods of visual disability while their cataracts mature. Among those subjected to the operation the complication rate will be slightly, but only slightly, higher than if the older methods are employed. If the cases are carefully selected the visual results in the large proportion of successful cases will be quite spectacular. As the acrylic lens is inserted in the position of, and has the same power as, the natural lens, the optical arrangements of the eye will be essentially unaltered, the retinal image will be of normal size, the field of vision full, there will be no prismatic displacement of objects and a normal and previously cataractous eye will be able to work in binocular harmony. In the majority of patients the eyes have excellent vision even without glasses, which are needed only to correct the—usually small—residual refractive error. Accommodation is, of course, lacking but the older patients are invariably accustomed to wearing either reading glasses or bifocals, whilst to the younger monocular cases the disadvantage of having to wear glasses for close work in which binocular vision is requisite, is negligible compared to that of having a virtually useless eye and no capacity for binocular vision at all.

CONCLUSION

The insertion of acrylic lenses has been practised for too short a time to make it certain that delayed complications may not occur, but few such have been recorded and, on the experience so far accumulated, it seems likely that the eye will tolerate within itself a foreign body of a suitable type, such as this, as readily as will many other tissues of the body. It would be wise, however, to reserve definitive judgment on this point for some years, during this time to practise eclecticism, and to remember that although the visual advantages accruing from the successful insertion of such a foreign body appear sufficiently great to counterbalance what we know so far of the extra risks involved, it is nevertheless not, and probably never will be, an operation universally applicable in cases of cataract.

CORNEAL GRAFTING

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'At the first sight they have changed eyes' (*Tempest* I **2**, 437)

Every clinic and consulting room has often heard the cry 'I know I have sight if only this film could be taken away'. Sometimes the implied hope can be fulfilled by so comparatively simple a matter as the removal of a cataract; in others a retinal lesion precludes the possibility; and in yet other cases it is in truth an opaque film in the cornea which prevents sight. The development of modern methods of corneal transplantation, or keratoplasty, has made possible the restoration of sight in many such cases.

A review of the records of 1,690 persons certified as blind showed that 170 were blind as a result of corneal lesions. It does not necessarily follow that all these would be suitable cases for corneal grafting, but certainly many would benefit by the operation. These figures do not, of course, take into account those who are blind from corneal lesions in one eye only and who are not certified.

HISTORY

It may be of interest to give a short review of the efforts and progress that have been made in the last century-and-a-half to replace the opaque cornea by a transparent medium.

At Montpellier, in 1789, de Quengsy put forward the suggestion that a scarred cornea could be replaced by a piece of glass similar to a watch-glass, but nothing came of the idea. During the first three decades of the 19th century attempts were made to replace an opaque cornea by an artificial pupil in the sclera but these openings soon closed over. Meissner tried to fill the scleral window with transplantation of an animal cornea, but unsuccessfully. Reisinger, in 1824, and Stilling, in 1836, advocated the transplanting of, respectively, the whole or part of an animal cornea. Then von Hippel, in 1877, published results of successful cases in which he had used his trephine, especially in non-penetrating grafts. Thirty years later Zirm reported a case in which the transplanted cornea had remained clear for three years. Elschnig of Prague began to use keratoplasty in 1908, and in 1926 I saw him perform several such operations using a small (about 2 millimetres) trephine. Some of the grafts remained transparent for, at least, months. Filatov published successful results in 1922 and was the first to use cadaver material. Tudor Thomas, as the result of much experimental work on rabbits, finally obtained clear grafts in 1930, and continued on human subjects. Modern instruments, drugs and methods were now at hand and progress was made in many countries.

Curiously enough, the pendulum seems to have swung back to de Quengsy

by a recent report of the successful insertion of a transparent acrylic implant into an opaque cornea (*Brit. med. J.*, 1953, **i**, 330).

THE DONOR

Even when the technique had been improved to such an extent as to offer promising results, the provision of an adequate amount of donor material was a retarding factor. Eyes which had been removed at operation were almost the sole source. Injured eyes are either too badly damaged or have begun to show signs of intra-ocular infection before removal; blind, painful eyes often have corneal opacities. The main source was from early cases of sarcoma of the choroid, fortunately not a common disease. Legal difficulties stood in the way of the removal of eyes from cadavers. In 1947, however, a law was passed in France authorizing the removal of eyes at necropsy, and this was followed by a great increase in that country in the number of corneal grafting operations, with consequent improvement in technique and the development of new methods. The case was put to the British public and Parliament. The idea was accepted without protest and in 1952 the Corneal Grafting Act became law. Before this, eyes or corneæ had been removed from the cadaver without legal sanction.

The Act provides that if any person expresses in writing, or orally before two witnesses, a request that his eyes be used for therapeutic purposes, the party lawfully in possession of the body after death may authorize the removal of the eyes for those purposes; and further, that the party lawfully in possession of the body may authorize the removal unless the deceased had before death expressed an objection, or a surviving spouse or relative objects to the eyes being so dealt with.

Already many persons have bequeathed their eyes in their wills; but as wills are often not disclosed until some time after death, the wish loses its value unless the donor's doctor is aware of it before death and, immediately upon the decease, establishes contact with the nearest eye hospital or ophthalmic surgeon doing this type of operation.

The most suitable eyes are those of an adult of middle age. The cornea is probably more inert than that of a child. The cornea must obviously be clear and free from scars and vascularity. The question has sometimes arisen as to whether or not the donor must necessarily have had a recent Wassermann test. The only cases in which spirochætes have been found in the cornea were those in which there was active keratitis and these would be automatically excluded. Corneæ from patients who have died from acute infective fevers or a virus disease should be excluded, but would rarely be presented.

The cornea or eye should be removed soon after death, if possible within two hours, before post-mortem changes have set in; although a cornea removed as long as twenty-four hours after death has been used with success. The whole eye may be removed and in this case the socket should be stuffed with cotton-wool to preserve the contour of the eyelids. It is not necessary to insert an artificial eye. Or the cornea alone may be removed with a Graefe knife completing, as it were, a complete cataract incision. The underlying

iris retains its lustre and colour, and the loss of the cornea, unless to the expert, may not be detected.

The eye when removed is hooked, or a suture loop is passed, through the sclera and suspended from the stopper in a wide-necked small jar above a small quantity of saline solution which keeps the atmosphere moist but does not macerate the eye. Corneæ are placed on a piece of lint in a vessel containing sterile liquid paraffin. This liquid is inert and there is no imbibition by the cornea. The donor material, if not to be used immediately, is stored in a refrigerator at a temperature of 4° C. and may be kept for five days or as long as three weeks.

The passing of the 1952 Act has made possible a recognized liaison between, on the one hand, medical officers of health, senior administrative medical officers, and hospital superintendents and, on the other, eye hospitals and departments, to facilitate the flow of material from the institutions and hospitals of which the former have administrative responsibility, to the surgeon's hand.

THE RECIPIENT

The conditions for which corneal grafting is applicable are those in which the disease or damage has been limited to the cornea; and in which there is every reason to suppose, by history and examination, that the other media of the eye are transparent and that the choroid, retina and optic nerve are healthy. Unjustifiable hopes and bitter disappointment may be prevented if the suppliant's doctor has explained this at an early stage, although the ultimate decision must be left to the surgeon.

Conditions generally considered favourable for transplantation are:—

(i) Interstitial keratitis, after the active phase.

(ii) Keratoconus in which optical treatment, even by contact lens, is ineffective.

(iii) Hereditary dystrophies or degenerations.

(iv) Small central or vascular scars.

A wide range of other conditions, even up to complete destruction of all normal corneal tissue by such agents as lime, glacial acetic acid and ammonia, have been operated upon with success or improvement of vision.

Contraindications are aphakic eyes, although cataract may be removed after a successful graft, and glaucoma. Youth or age does not, in itself, contraindicate operation.

General indications.—(a) Optical, with a view to improving the visual acuity.

(b) Preparatory, on a grossly damaged and vascular cornea to prepare the ground for an optical graft.

(c) Therapeutic, employed largely by the French school in cases of active and progressive diseases of the cornea, such as neurotrophic and tuberculous keratitis in which the usual treatments are of no avail and perforation is feared. Filatov drew attention to the trophic action of corneal grafts.

(d) Tectonic (τεκτων: builder), applied by the French school to keratoplasty in such cases as corneal fistula and recurrent symblepharon.

(e) Cosmetic.

It will be noted, in passing, that the operation has been employed in a wider range of subjects by the French school, due largely to its comparative wealth of donor material.

THE GRAFT

Shape and size.—The graft may be rectangular or disciform. The rectangular technique has developed in the U.S.A. owing to the fact, it has been stated, that their instrument-makers were late in perfecting the circular trephine. The circular graft is now favoured by most surgeons. It is cut by a trephine, the most popular model of which is the Franceschetti trephine (fig. 1) made in Switzerland and obtained only with difficulty in the United Kingdom. This is made in various sizes, from 5 to 9 millimetres in diameter. The 5 or 6 millimetre graft is most in favour. Some surgeons advocate a graft 0.1 millimetre larger than the aperture in the recipient's eye, whilst others support the use of the same trephine for the donor and recipient cornea.

FIG 1.—Grieshaber Franceschetti trephine (actual size).

Thickness.—(i) *Penetrating graft*, in which the whole thickness of the cornea is replaced. This method must, of course, be employed when the deepest layers of the cornea are involved (fig. 2).

(ii) *Lamellar*, in which superficial layers of the cornea are removed, the thickness depending upon the corneal opacity and the total thickness of the cornea shown by slit-lamp examination. The technique of this method is more difficult but it is not fraught with the same danger of immediate and postoperative complications. Its particular indications are in only eyes and aphakic eyes, and as a preparatory and therapeutic operation (fig. 3).

FIG. 2.—Penetrating graft for deep opacity.

FIG. 3.—Lamellar graft for superficial opacity.

THE OPERATION

Preoperative preparations

The preparation of the patient is, in general, that which is carried out before any intra-ocular operation: infection of the lids, conjunctiva and lacrimal sac must be dealt with. Symblepharon, a frequent concomitant of damage to the eye by lime or other corrosive agents, may be dealt with previously by the 'tunnel' operation (Reid, A. M. (1933): *Trans. ophthal. Soc. U.K.*, **53**, 592), and no fibrotic strands must remain to exert tension upon the limbus or cornea. The anæsthetic may be either general or local,

with appropriate premedication. Akinesia is important in local anæsthesia. The orbicularis is immobilized with a facial nerve block and the four recti injected with novocain. Retrobulbar injection tends to lower the intra-ocular tension, and makes trephining more difficult. Contraction of the pupil with eserin minimizes the risk of damage to the lens by the trephine.

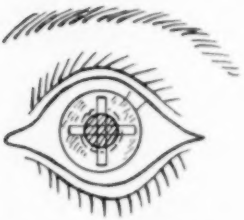

FIG. 4.—Bridge-sutures over graft and egg-membrane.

Operation proper

The following is a description of the technique which I use.

(i) *Marking out the corneal disc and placing the sutures.*—The lids are retracted with sutures, and fixation sutures are passed through or under the tendons of the superior and inferior recti.

The cornea is measured and the centre scratched with a needle and marked with fluorescin. The limits of the trephine cut are marked from the centre. The trephine is placed in position with rigid insistence that its axis is throughout held normal to the corneal surface. The trephine cut is now made sufficiently deep to mark the circle and to make a bed for the trephine when it is re-applied. The circle is marked with fluorescin. Double bridge-sutures of Kalt's silk are inserted into the cornea with No. 5 Grieshaber needles, the loose ends lying inferiorly and temporally for convenience in tightening and tying (fig. 4). The eye is then closed while the graft is being prepared.

(ii) *Preparation of the graft.*—At a separate table, previously prepared, the donor eye is taken up, washed in cetavlon, 1 per cent., and bound circumferentially with a strip of gauze to prevent slipping. It is then held, cornea horizontal and with adequate pressure exerted, by an assistant. The centre is marked as in the recipient cornea. The same trephine, with the piston well retracted, is applied with equal attention to its vertical position and with even, firm, rotary movements with a wide excursion the disc is cut. If the trephine is sharp, the disc will be clearly cut and will lie in the barrel of the trephine from which it is extruded by the piston and laid on a watch-glass covered with a saline-dampened piece of gauze.

A disc of egg-membrane from a hard-boiled egg is then cut with another trephine, 1 millimetre larger in diameter. Radial notches are cut with scissors at the edge of the membrane to allow it to approximate to the cornea. The egg-membrane is placed on the watch-glass.

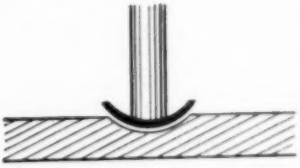

FIG. 5.—Punching out graft from excised cornea on wax slab. (Amsler's method).

The graft, as has been mentioned earlier, may be cut from an excised cornea and not from a whole eye. A slab of paraffin wax is taken and a small saucer-shaped indentation made with the heated testing-plate of a Schiötz tonometer. The cornea is placed, epithelium down, in the depression. The trephine is held vertically and with a firm downward thrust, without rotation, the corneal disc is punched out (fig. 5).

(iii) *Removal of the disc from the recipient's cornea.*—The piston of the trephine is now set so that the free part of the blade is of the estimated thickness, but no more, of the recipient cornea. The corneal sutures are spread away from the disc. The trephine is placed accurately and again vertically on the marked circle, the eye is held steady by the tendon sutures, and the trephine rotated as before. If the trephine is held vertically there is little fear of aqueous escaping between the trephine and the cornea, and the piston prevents escape within the trephine, so that the cut can be completed or almost completed without loss of aqueous. When the trephine is removed the section is not always complete and the disc may be held by a hinge. The

trephine cannot be re-applied and the hinge of endothelium and Descemet's membrane is cut through with fine scissors or a knife. If a tag of cornea remains attached to the edge of the hole it is held by de Saint Martin forceps and cut off.

(iv) *Placing of the graft.*—The graft is lifted on a small spoon and slid into position guided by an iris repositor. With the same instrument it is gently pressed until the surface of the graft is flush with that of the recipient's cornea. The egg-membrane is now placed over the graft. The sutures are replaced over the centre of the cornea and gently and firmly pulled into place with equal tension on all four ends of the sutures. They are then tied.

On no account must the pupillary margin come into contact with the junction circle before the anterior chamber is re-formed; otherwise anterior synechiæ may occur. It is easier to keep a pupil fully dilated than contracted and so a subconjunctival injection of mydricain is given and atropine is instilled to ensure full and continued dilatation until the first dressing.

Penicillin ointment is applied to the cornea, the eye is closed and a *tulle gras* disc applied to the eyelids. A pad is placed over both eyes and a bandage, which is firmer than strapping, is applied over both eyes.

FIG. 6.—Trephine applied to cornea. Black silk sutures under tendons of superior and inferior recti.

(v) *Lamellar keratoplasty.*—The foregoing description applies to penetrating keratoplasty and must be modified in the case of lamellar grafting. In this case the position of the recipient's disc is marked out as before and the trephine piston is set to a depth estimated to carry the cut to the lowest level of the opacity. The edge of the disc is then grasped with de Saint Martin forceps and the disc dissected off with a narrow straight keratome or other suitable knife, care being taken to keep in the same tissue plane throughout. Blunt dissection may be used. Bridge sutures are inserted as for a penetrating graft. The donor's cornea may be cut in the same way; or a deep corneal cut made with the trephine and a Böck knife which holds a thin Gillette blade used, as in skin grafting, to take from the cornea a large slice out of which the already demarcated graft-disc falls.

If a lamellar graft is to be cut from an excised cornea, the finger of a rubber glove is filled with Dunlopillo material and the cornea stitched to the convex tip (Williamson Noble (1952): *Brit. J. Ophthal.*, **36**, 221).

(vi) *Other methods of fixation of the graft.*—Many modifications in the pattern of bridge sutures are used but two other methods of fixation have been introduced more recently—splints and direct suture. (a) Splints: A contact lens sutured to the cornea, or without sutures; Pittar's tantalum splint; Stallard's transparent disc-shaped splint; and rubber and cellophane discs all have their advocates. (b) Direct suture: Direct suturing of the graft to the recipient cornea has become a feasible proposition with the advent of the fine Grieshaber needle. It is used where the graft is in danger of displacement or has actually become displaced, but some surgeons employ it as a routine measure. The sutures are placed through the cut edges of the graft and cornea so that the suture material does not come into contact with the aqueous.

Postoperative treatment

(i) *Nursing.*—The patient is kept strictly in bed with as little movement as

possible for twenty-four hours. The first dressing is done in forty-eight hours; the eye is not inspected unless there is a complaint of pain but the lower lid is pulled away from the eye and 1 per cent. atropine drops are instilled. Futher similar dressings are done every second day. On the tenth day the corneal sutures are removed and the other eye left uncovered.

(ii) *Radiotherapy.*—The invasion of the graft by new blood vessels from the recipient cornea can militate against the success of a technically perfect operation. Radiotherapy in appropriate doses destroys the endothelial cells and causes obliterative endarteritis. It can also be employed preoperatively to reduce vascularity. It may be applied by (a) x-rays or (b) radium. (a) X-rays.—Soft radiations from a 60 kV Chaoul apparatus, without added filter, are applied to the cornea for 20 seconds giving a dose of 50r units. The first treatment is given about ten days after the operation and repeated weekly for a total of six treatments. (b) Radium.—Beta-ray is the effective agent and is applied by a 10-milligramme radium-D applicator. This method is largely used in the United States and in France but it is considered by some radiotherapists in this country to be too caustic and not sufficiently capable of control.

FIG. 7.—Bridge-sutures over egg-membrane, 8th day. The silk at nasal side is the free end of a direct graft-cornea suture.

(iii) *Cortisone* is not used as a routine measure but in the treatment of complications including vascular invasion; and not earlier than a week after the operation. It is given in the form of drops or subconjunctival injections of 0.2 ml.

Complications

Immediate.—(a) Damage to lens—this can be avoided by meiosis, by vertical placing of the trephine and by setting the piston at the correct depth to prevent escape of aqueous. (b) Bad centring of graft and eccentric crossing of bridge sutures—avoided by accurate measurements. (c) Poor coaptation and tilting of graft; avoided by vertical trephining of recipient and donor corneæ. Treated by graduated pressure pads or by direct suture of graft to cornea. (d) Presentation of vitreous, a rare occurrence, calls for direct suture. Loss of lens matter may call for evacuation of the lens.

Later complications.—(a) Delayed formation of anterior chamber.

(b) Infection: prevented by strict asepsis. Treated by usual methods.

(c) Œdema due to imbibition of aqueous by the graft. Faulty coaptation or insufficient fixation of the graft is partly responsible for this.

(d) Anterior synechiæ are due usually to insufficient mydriasis to pull the iris margin away from the graft-cornea junction. Regrafting may be necessary.

(e) Glaucoma may be due to anterior synechiæ which should be divided. Further treatment by filtering operation.

(f) Vascularization of the graft, if not too rampant, may be amenable to cortisone or radiotherapy. It is nearly always associated with a vascular receiving cornea which should have been dealt with before the main operation by one of the following procedures: (i) *Peritomy or peridectomy* in which a 2-millimetre zone of sclera is cleared around the limbus and the severed conjunctiva sutured to the sclera beyond the zone. The actual cautery is applied to patent vessels at the limbus. This often reduces the vascularity of the recipient cornea. (ii) *Superficial keratectomy* in which fleshy vascular tissue, if confined to the surface layers, is dissected off and the exposed raw surface covered with amniotic membrane. This may result in a cornea sufficiently avascular to accept a graft. (iii) *Preliminary lamellar keratoplasty*.

(g) Opacification of the graft. This may be due to poor coaptation of the graft so that its nutrition is not established, or to extension into the graft of still active disease of the receiving cornea. Here again, cortisone sometimes achieves success, but on the whole the prognosis is poor and another operation may have to be considered.

(h) Maladie de greffon is an elusive condition, of obscure etiology. It begins after the surgeon and the patient have begun to congratulate themselves and each other upon a successful result—perhaps three weeks after the operation. Epithelium and substantia show opacities, Descemet's membrane is thrown into folds and the surrounding receptor cornea becomes vascular. The much abused allergy may be the miscreant. The whole gamut of therapy may be called into play without success, until a second graft is eventually done.

THE FATE OF THE GRAFT

The point at issue is whether the graft acts merely as a scaffolding upon, and into which, the receptor cornea builds its own tissue, or whether the graft retains its own identity accepted urbanely by the host until, in course of time, its cells and acellular tissue are replaced, with those of the host, through normal metabolic processes. The consensus of opinion is that the epithelium and endothelium (cellular structures) are rapidly replaced. In a recent case of mine the epithelium of the graft was a loose sheet, stuck to the piston of the trephine and almost completely separated from the underlying tissue. Had another eye been available the graft would have been discarded. The graft was quickly epithelialized by the host cornea and the result was uncomplicated and favourable.

Bowman's and Descemet's membranes and the stroma remain. Recent work on animals has shown that the nerve fibres degenerate in the graft and

as far as 2 millimetres in the surrounding cornea but that in twenty-eight weeks nerve fibres, without their sheaths, have entered and innervated the whole graft. Clarity or opacity of the cornea or graft is not in any way dependent upon the presence or absence of nerve supply.

RESULTS

The criteria are transparency of the graft, visual acuity and, in the case of therapeutic grafts, the amelioration of the morbid process. An American report states that when there is a proper selection of cases, a high percentage of clear grafts can be obtained. The question is what is a proper selection of cases? The patient whose vision is improved from the 'perception of light only' to 6/60 is often more satisfied with the improvement in his condition, than the patient with a central corneal scar whose visual acuity is improved from 6/24 to 6/6. To refuse patients in whom the prognosis is poor may improve statistics, but condemns to blindness some who might be relieved. Figures from different sources show considerable variation but, taking all cases, 40 to 50 per cent. show improvement, whilst in favourable cases this figure rises to 70 per cent.; between 10 to 20 per cent. are made worse.

FIG. 8.—Penetrating graft: case of interstitial keratitis. The upward-looking eye makes the graft appear eccentric. V. A. improved from 1/60 to 6/18.

CONCLUSION

A brief review of the history of keratoplasty has been given; problems regarding donor material have been alluded to; and the scope of, and indications for, various forms of keratoplasty have been mentioned.

Many different operative methods are practised by different ophthalmic surgeons but, to avoid confusion, only one method has been described in detail.

Before a decade has passed, statistics of results will undoubtedly present a better picture which will indicate that more of our fellow-men have regained ' that one Talent which is death to hide'.

The phographs for figures 6, 7 and 8 were taken by the Central Photographic Department of the University of Liverpool, the block for figure 1 was supplied by Theodore Hamblin Ltd., and the line drawings by the author.

TOXIC AMBLYOPIA

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Although the term 'toxic amblyopia' is generally used as referring to those forms of partial blindness which are caused by external poisons, the relationship between certain forms of exogenic amblyopia, such as that caused by tobacco, and various disorders of metabolism or of nutrition, is so close that it seems rational to include both exogenic and endogenic factors in a review of this subject. Whether the causal factor be exogenic or endogenic, or a combination of both, the term toxic amblyopia refers purely to those forms of impairment of vision caused by toxins which affect the fibres of the optic nerves or their ganglion cells. Various poisons may, of course, cause 'blurred vision' by altering the refraction of the lens or by impairing the power of accommodation. With these, however, we are not concerned.

From the point of view of disturbance of visual function, the various types of toxic amblyopia may, broadly speaking, be divided into two groups, those in which the predominant effect is upon the peripheral portions of the field of vision, and the much larger group, in which the disturbance mainly affects central vision. In the first group are poisons such as quinine, certain of the organic arsenicals, filix mas, salicylates, ergot, amidobenzol (anilin) and nitrobenzol, dinitrobenzol and trinitrotoluol. In the second group are amblyopia from causes such as tobacco, alcohol, certain of the inorganic arsenicals, lead, carbon disulphide, and also those cases which occur, for example, in diabetes and in pernicious anæmia. In addition, there are those forms of amblyopia generally classified under the heading of 'nutritional neuropathy'.

POISONS PREDOMINANTLY AFFECTING THE PERIPHERAL FIELD OF VISION

Quinine.—Although amblyopia as a result of quinine poisoning is relatively rare, cases still occur. Whilst 1 grain may cause transient blurring of vision in a susceptible person, most cases of severe quinine poisoning follow the taking of 30 grains, or more, within a 24-hour period. The majority follow the taking of a large dose as an abortifacient. An interesting case, however, has been recorded (Foster Moore, 1925) of a man who developed optic atrophy after drinking two bottles of a proprietary orange and quinine wine.

Tinnitus and deafness, usually lasting a few hours, precede the onset of visual failure. In very severe cases the patient may temporarily be completely blind, with widely dilated, fixed pupils. Within a few hours the fundi appear pale with retinal œdema, and this is succeeded by gross constriction of the retinal arteries and their branches.

Although permanent blindness has never been recorded as a result of

quinine poisoning, the degree of recovery is variable. Improvement may occur within a few days or may be delayed for several weeks. As some central vision returns, one is able to test the visual fields which are found to be grossly constricted. In severe cases there is marked constriction of the peripheral field (fig. 1), causing the patient to be quite unable to get about even although central vision, as tested by the ability to read small print, may have returned to normal. In most cases there is a large measure of further recovery but, in nearly all, some permanent contraction of the field remains. In all but the most severe cases the degree of residual constriction will not be disabling, except perhaps in dim light. Several months may elapse before the final degree of recovery is reached.

Of the other poisons which may cause a type of amblyopia similar in some respects to that produced by quinine, little need be said apart from recording,

FIG. 1.—Extreme contraction of the peripheral fields of vision such as may occur in the acute stage of quinine amblyopia.

very briefly, some of the circumstances in which such poisoning may occur.

Salicylates.—The ocular symptoms are similar to those produced by quinine, but are less severe and more transient. In general, poisoning from salicylates only results from large doses and recovery is usually rapid. For example, a case has been recorded (de Schweinitz, 1896) in which a girl of sixteen years of age consumed a total of 8 g. of sodium salicylate, in ten doses each taken hourly, and then fell asleep. Although she was completely blind when she awoke, the visual acuity had returned to normal within twenty-four hours.

Organic arsenicals.—Organic preparations of arsenic can be highly toxic to the visual elements, some of the pentavalent preparations being particularly dangerous. For example, in days gone by, a large number of cases of permanent blindness resulted from treatment with preparations such as atoxyl. Even a relatively non-toxic preparation such as tryparsamide must be used with caution, and it should not be used without preliminary, and repeated, examination of the optic discs and visual fields.

On the other hand, the trivalent arsenicals, such as salvarsan, neosalvarsan,

and sulphostab are all less toxic than the pentavalent drugs. Even the trivalent arsenicals, however, should never be given to children, since the visual fields cannot be checked, and severe impairment of vision has been recorded following their use.

Although in some cases there may be sudden and complete blindness, the more usual effect is that of an acute contraction of the peripheral field of vision, just as in a severe case of quinine poisoning, but with the important difference that there is little or no tendency to recovery.

Filix mas may, on rare occasions, cause amblyopia similar to that produced by quinine, one peculiarity being that the visual impairment is not uncommonly unilateral.

Ergot, given in large doses, has a similar effect to quinine, but the amblyopia is transient.

Amidobenzol (aniline) and nitrobenzol, both of which are used in the dyeing industry, and *dinitrobenzol and trinitrotoluol*, which are used in the manufacture of explosives, may also produce toxic amblyopia. A case has also been reported of bilateral optic neuritis, with constriction of the retinal vessels, retinal hæmorrhages, and constriction of the visual fields, after the use of hair dye. If the workers are removed from contact with the chemical concerned, full recovery of visual function takes place.

POISONS PREDOMINANTLY AFFECTING THE CENTRAL PORTIONS OF THE FIELDS OF VISION

In the second, and much the larger, group of cases of toxic amblyopia are included poisoning by substances such as tobacco, alcohol, certain of the inorganic arsenicals, and also those cases which occur in diabetes mellitus and in pernicious anæmia. In addition, it is proposed to include in this discussion those cases generally classified under the heading of 'nutritional neuropathy'.

TOBACCO AMBLYOPIA

Partial blindness resulting from the use of tobacco is by far the most common type of toxic amblyopia met with in Great Britain.

The patient is usually a man of between 50 and 60 years of age. The onset is insidious, with gradual difficulty in reading small print, and the patient will often state that, at first, he thought that he simply needed stronger spectacles. As the condition progresses he will commonly complain of a mist before his eyes, and that he cannot recognize his friends in the street. He may often volunteer the information that he sees better in dim light, and that bright light dazzles him. If he drives a car, or if he is an engine-driver, he may complain that he cannot see red signal lights. The recognition of tobacco amblyopia is, therefore, of particular importance in the case of men whose work entails the recognition of coloured signals.

The vast majority of cases occur in men who are pipe-smokers. Occasion-

ally it affects those who smoke cigars but, certainly in this country, there are now probably few who can afford to smoke a sufficient number to run any real risk of their sight becoming affected. The condition is rarely seen as a result of cigarette smoking. If questioned regarding the amount of tobacco consumed the patient will usually state about 2 oz. a week. One will often find, however, that he has, of his own accord, recently cut down his smoking, and that his average consumption was formerly 3 to 3½ oz. a week.

In severe cases visual acuity may be reduced to 3/60 in each eye; in more moderate cases to, say, 6/36 or 6/24. In most cases both eyes are, more or

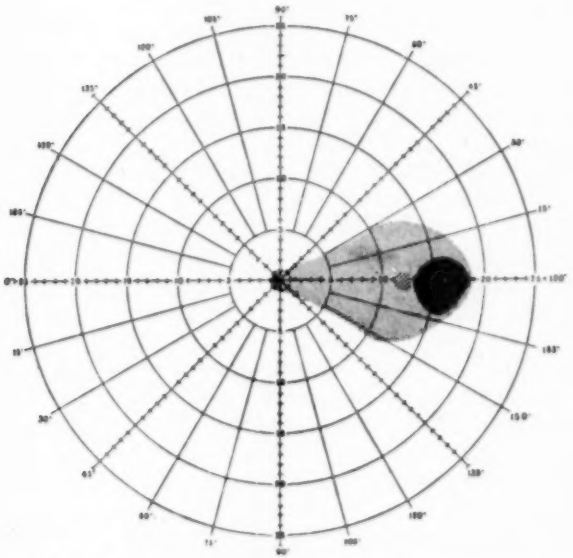

FIG. 2.—Tobacco amblyopia. Centro-cæcal scotoma to a 20 mm. red test object. Small dense nucleus, within the main scotoma, near the blind spot.

less, equally affected but, occasionally, the acuity may be, for example, 6/24 in one eye and 6/9 in the other. In such cases the most noticeable disturbance will occur on reading small print at ordinary reading distance.

If the field of vision is examined, a characteristic scotoma will be found, extending from the blind spot to the point of central fixation. The scotoma begins as an outgrowth from the nasal side of the blind spot, the defect then gradually enlarging to reach, and then embrace, the fixation area. Even in cases with relatively little failure of vision as tested on the ordinary test card, there will be a well-marked centro-cæcal area in which, for example, a 10 mm. red test object will be seen less distinctly than on the other side of

the fixation area. Only when the scotoma actually encroaches on the fixation point will the patient notice a real difficulty in reading.

There are two characteristics of the scotoma which never seem to occur in any other condition. The first is the presence of one or two areas of greater intensity, within the main scotoma. The second feature lies in the ill-defined nature of the edges of the scotoma, which is often difficult to chart with accuracy. In addition, the defect for colour is far greater than that for white (fig. 2).

The influence of alcohol and of disturbance of the general health.—In the United States of America, toxic amblyopia in those who smoke heavily and also drink to excess has for long been regarded as being mainly due to the ill-effects of alcohol. In so far as this country is concerned, there seems to be no doubt that tobacco amblyopia is a definite clinical entity and that alcohol, if consumed, only acts as an aggravating factor in depressing the general health.

In a survey of cases of severe 'tobacco-alcohol' amblyopia in the United States, Carroll (1937) produced remarkable cures as a result of intensive administration of the whole vitamin B complex, the patients being hospitalized during treatment and consuming their normal quantity of alcohol and tobacco. He therefore suggested that the primary factor was a nutritional one, rather than a true toxic effect from the alcohol or tobacco. Against this, however, is the definite clinical fact that a true tobacco-amblyopia scotoma never seems to occur, even in patients with diseases such as pellagra or beri-beri unless, at the same time, they also smoke tobacco. Again, whilst alcohol may produce acute blindness and peripheral neuritis, there seems to be no such thing as pure chronic alcohol amblyopia, and peripheral neuritis does not occur in cases of pure tobacco amblyopia.

To sum up, therefore, there seems to be no doubt that some volatile product in tobacco can act as a definite poison, in so far as visual function is concerned. On the other hand, any depression of the general health, or disturbance of nutrition, may be the immediate cause of symptoms appearing in one who has long smoked without any apparent ill-effects.

Treatment.—In certain cases, measures designed to improve the general health, and in particular to ensure an adequate intake of vitamin B, may be sufficient to enable the patient to resist the poison he is consuming. In most cases, however, only a complete cessation of smoking will suffice to effect a cure. In so far as tobacco amblyopia in this country is concerned, it is wise therefore to advise the patient to stop smoking completely. In cases of any severity, however, and especially if there is any doubt whether the patient has in fact completely stopped smoking, it is probably wise to give large doses of the whole vitamin B complex.

Prognosis.—During the first few weeks after cessation of smoking, it is not uncommon, owing to the cumulative effect of the poison, for the symptoms to increase, and the patient should be warned that this may occur.

In mild cases improvement usually begins in about six weeks, and is well established in two to three months. In more severe cases improvement will be slower.

DIABETES MELLITUS

Although cases of chronic bilateral optic neuritis have been described as occurring in diabetics it is, I think, doubtful if there is such a thing as a true diabetic optic neuritis. On the other hand, I have seen several cases of tobacco amblyopia develop during a phase of incomplete control of the diabetic state, and resolve completely, without cessation of smoking, as soon as control was regained. I know of one patient, a heavy smoker, who develops such amblyopia periodically, and if his period of poor control is prolonged, he cures his tobacco amblyopia by stopping smoking. If he recovers control rapidly, however, his amblyopia disappears without any alteration in his smoking habits. Bilateral toxic amblyopia in a diabetic patient should, therefore, always arouse suspicion of the possibility of tobacco amblyopia in a patient who smokes a pipe or cigars.

AMBLYOPIA IN PERNICIOUS ANÆMIA

Amblyopia as a complication of pernicious anæmia is a relatively rare occurrence although a number of cases have been recorded from time to time. Cohen (1936) was the first to draw attention to the fact that visual failure might be the presenting sign in pernicious anæmia, and that this might occur when there were only slight changes in the blood picture and no other evidence of disease in the central nervous system. He recorded two cases of this type which responded to liver therapy with practically complete recovery of vision. More recently, Turner (1940) has recorded three cases, in all of which considerable recovery of vision occurred following liver injections. As Turner has emphasized, the return of vision under treatment is usually slow and may not be quite complete. It is also noteworthy that in his first two patients the visual failure was the first symptom of which the patient complained.

In toxic amblyopia, or optic neuropathy, occurring as a complication of pernicious anæmia, the onset is slow and usually steadily progressive. A certain degree of optic atrophy develops which is quite definitely more marked than in a case of, for example, tobacco amblyopia of similar severity, in so far as visual impairment is concerned. The usual field defect is a central scotoma, which may be quite small and difficult to chart if the examiner is not expert in perimetry. Occasionally the scotoma may be centro-cæcal in position. In the latter event one should again always be on the alert to make sure that one is not, in fact, dealing with a case of tobacco amblyopia. As we have already seen, the scotoma in tobacco amblyopia is diffuse, with ill-defined edges, and often has one or more nuclei within it. In pernicious anæmia, the scotoma, whether it be central or centro-cæcal in

position, is dense, and has well-defined edges. This differentiation, by accurate perimetry, is of some importance since, except in early cases, the prognosis is better in tobacco amblyopia than in the true neuropathy complicating pernicious anæmia.

I have seen several cases, diagnosed as optic neuritis complicating pernicious anæmia, which were in fact cases of tobacco blindness, and my own view is that some of the cases described in the literature as responding well to liver therapy were, in fact, probably examples of tobacco amblyopia.

'NUTRITIONAL NEUROPATHY'

In recent years great interest has centred around the subject of a nutritional 'syndrome' which was seen among prisoners in the Middle East and in the Far East during the recent war.

This syndrome has been described by various authors, and a brief

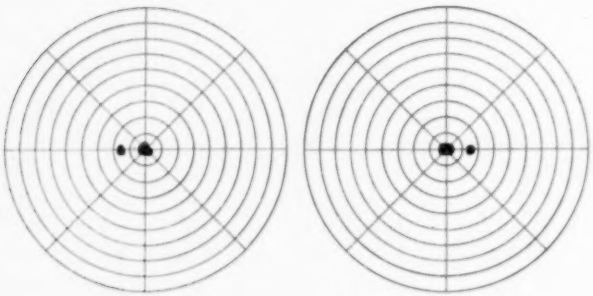

FIG. 3.—Nutritional optic neuropathy : dense central scotoma.

description of those cases encountered in the Middle East (Spillane and Scott, 1945) will demonstrate the essential symptomatology. The complete syndrome consists of optic neuropathy, nerve-deafness, ataxic paraplegia, and vocal cord paresis, but many patients develop only the visual impairment. In the majority of cases the onset is gradual over a period of months. In about 54 per cent. there was optic neuropathy without other signs, and less than 5 per cent. failed to develop visual trouble. In about 20 per cent. the optic neuropathy was associated with nerve-deafness.

In a case of moderate severity the central or paracentral scotoma, which became evident on perimetry (fig. 3), in many ways resembled the defect met with in cases of pernicious anæmia. The neurological signs, present in nearly one-third of the patients, were essentially those attributable to changes in the posterior column of the spinal cord. Numbness and tingling of the legs or a burning sensation in the soles of the feet were the most common early complaints. The earliest objective sign was a loss of vibration sense. Although obvious ataxia was only present in about 14 per cent.,

early ataxic signs and evidence of posterior column changes were present in about 30 per cent. of the cases. Whilst those cases occurring in the Far East were complicated by the coexistence of multiple deficiencies, for instance, pellagra or beri-beri, the prisoners-of-war in the Middle East appeared in good general health, although significant loss of weight and complaint of general fatigue on exertion were common. Skin, heart and lungs were not affected, but diarrhœa was a common complaint.

CONCLUSIONS

In this brief survey of the subject of 'toxic amblyopia' it has been shown that at one end of the scale are examples of pure exogenous poisoning, as exemplified by quinine amblyopia.

Secondly, come tobacco and tobacco-alcohol amblyopia in which, whilst there is no doubt that the visual elements are affected by some exogenic poison, the general health of the patient, and in particular the question of adequate intake of vitamin B, are important factors in the development and treatment of the condition.

Finally, there are the more truly 'nutritional' neuropathies as exemplified by that occurring in the 'nutritional syndrome', which has been discussed. To what extent some unknown toxic factor may also be at work in the latter group must, in the present state of our knowledge, remain an open question. One point of great interest is that this 'nutritional' syndrome rarely seems to occur under conditions of acute starvation. As Spillane (1947) has said, 'in early days war brought famine, in our time the danger is not so much starvation as malnutrition'.

We see, therefore, that whilst certain forms of amblyopia are due purely to external poisons, in the majority there is probably a combination of factors at work, and that certain toxic substances, such as volatile products of tobacco, may cause impairment of vision in the presence of subclinical nutritional deficiency which would not occur if the individuals were in a state of good general health.

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THE SOVEREIGN AND THE SURGEON

By Sir ARTHUR S. MacNALTY, K.C.B., D.M., F.R.C.P., F.R.C.S.
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The Book of Ecclesiasticus exhorts us to honour a physician (and in this sense it equally means surgeon) with the honour due unto him and adds: 'For of the most High cometh healing, and he shall receive honour from the King'.

On May 5, 1953, Queen Elizabeth II is to lay the foundation stone of the new buildings of the Royal College of Surgeons, which are to rise like a phœnix from the ashes of the old to mark a new epoch in its history. By this gracious act Her Majesty has honoured English surgery anew, for as Princess Elizabeth, in 1951, she consented to become an Honorary Fellow of the College, as did her great-grandfather, King Edward VII who, as Prince of Wales, in 1900 became the first Honorary Fellow. Other royal holders of this distinction are Queen Elizabeth, the Queen Mother, the Princess Royal and the Duke of Gloucester. It has also been accepted by the late Duke of Connaught, the Duke of Windsor when Prince of Wales, and by the Earl of Athlone. His Majesty King George VI graciously assumed the office of Visitor in 1944.

In honouring English surgery Her Majesty is following the tradition of her ancestors who, since the sixteenth century, have fostered and encouraged this art and science. Examples of this royal interest will emerge from this article, which endeavours to sketch the history of the Royal College of Surgeons.

THE BARBER-SURGEONS' COMPANY

Even as early as the fourteenth century the English surgeons were making contributions to knowledge. The first of them appears to have been John Arderne, who wrote an excellent account of the signs and symptoms of carcinoma of the rectum. The barbers practised surgery, and the striped red and white barber's pole is emblematic of their blood-letting and bandaging.

The Barbers' Company of London is first noted in the City's records in 1308. There was a rival Company known as the Fellowship or Guild of Surgeons, which had power to report the faults of unskilful surgeons. After years of struggle for supremacy of authority in the practice of surgery, the two Companies entered into alliance with one another in 1493.

King Henry VIII suffered from varicose ulcers of the legs and derived much benefit from the ministration of his surgeons. Thomas Vicary, his Serjeant-Surgeon, Master of the Barbers' Company, four times Master of the Barber-Surgeons' Company, Surgeon to St. Bartholomew's Hospital, and England's leading surgeon from 1527 to 1562, undoubtedly impressed

upon the king the importance of organizing the profession of surgery and elevating its status, as he had already done for the sister science of medicine by founding the College of Physicians in 1518.

In 1540, Henry VIII enacted (32 Hen. VIII, c. 42) that the two distinct Companies of Surgeons in London, one called the Barbers of London and the other the Surgeons of London, should from thenceforth be united and

FIG. 1.—H.M. the Queen with the President, Sir Cecil Wakeley, when as Princess Elizabeth she received the Honorary Fellowship.

made one Body Corporate to be called by the name of the Masters or Governors of the Mystery and Commonalty of the Barbers and Surgeons of London. Although Vicary was not Master of the Barbers' Company at that time, his major share in effecting the union is indicated in Holbein's famous

picture which shows the king handing the Act of Union incorporation to him. Henry further showed his interest by presenting the Company with a drinking-cup and cover, in silver gilt, beautifully chased.

Henry was generous and grateful to his surgeons. He granted to Vicary tithes of grain and glebe lands at Boxley, Kent. Another of the king's surgeons was Sir John Ayleff, Master of the Barbers' Company in 1538. He treated Henry for a fistula, 'for which the King bestowed on him a great estate in gratitude'. Ayleff was also surgeon to Edward VI, who made him a knight: the first English surgeon, so far as I am aware, to receive the accolade, and an indication of the high professional status which surgeons had now acquired. Henry's surgeons, Richard Ferris or Ferrers, who attended the king in his last illness, John Motforde or Mumford, and Ayleff each received legacies of 100 marks in Henry's will, and all held high office in the Barber-Surgeons' Company. Harry Mackerel, King Edward VI's surgeon, in 1549 received a grant of land in Kent from the king, being joined in the patent with 'old Vicars' (Thomas Vicary) (*Cal. of State Papers, Domestic*, 1547-1580, p. 14. Warwick to Cecill).

The Barber-Surgeons' Company promoted the teaching of anatomy and surgery;* as a result, operative surgery became more dexterous and resourceful. In lithotomy, improvements were made in the use of the staff and other instruments. A 'radical' cure of hernia superseded the application of the actual cautery; operation for stricture of the urethra was improved; plastic operations were done; and ophthalmic surgery was taken to some extent out of the hands of quacks. On the instructions of the Company, John Halle of Maidstone, a contemporary of Vicary, evicted quacks from that district by searching medical examinations. He wrote a book, entitled 'Historical Expostulation against the Beastlie Abusers of Chirurgery and Physick in our Time'.

Thomas Gale and William Clowes (*c.* 1544-1604), surgeon to Queen

*The Barber-Surgeons set a high standard of education in surgery. After 1540, the intending surgeon on leaving a grammar school at the age of twelve or thirteen had to attend at the Company's Hall in Monkswell Street for a personal interview. There the Masters of the Mystery satisfied themselves that the applicant was not deformed or suffering from any chronic disease and that he knew Latin. If satisfied, his indentures were signed and sealed and he was apprenticed to a surgeon for seven or nine years. At the end of apprenticeship he attended at Barber-Surgeons' Hall to undergo an examination. This was called 'the first preferment of grace' and gave him a limited licence to practise. After further experience he could proceed to Master of Anatomy and Surgery, 'the second preferment of grace', by reading a thesis before the Company every six months or by undergoing periodical re-examination. The Mastership gave him a permanent licence to practise. He could then either apply for the Bishop of London's licence or the 'Great Diploma', the highest qualification in surgery granted only to a select few. The Wardens and Masters of the Company were obliged under penalty of a fine to attend the demonstrations in anatomy and the lectures on surgery given in their Hall. There were also annual 'public anatomies' which lasted for three days, at the end of which there was a banquet.

Elizabeth I and to St. Bartholomew's Hospital, by their writings and teaching improved surgical knowledge.

The first Barber-Surgeons' Hall in Monkswell Street is said to have been of the date of Edward IV. The second hall was built by Inigo Jones in 1636, and was repaired by a distinguished amateur of architecture, the Earl of Burlington. The anatomical theatre was one of the finest of Inigo's works.

FIG. 2.—Henry VIII handing the Act of Union to the Barber-Surgeons' Company, 1540. (*After the painting by Holbein at the Royal College of Surgeons.*)

The Hall survived the Great Fire of London, but was destroyed by the Luftwaffe in 1941.

James I, in a letter to the Company written from Newmarket and dated 1617, requested the loan of the Holbein picture in order that it might be copied. In the nineteenth century a similar request was made by Prince Albert who kept it at Buckingham Palace for a month. Charles I, in 1625, gave the Barber-Surgeons a Charter confirming Henry the Eighth's Charter and further empowering the Corporation to appoint Examiners of Surgeons in London, and the right to examine surgeons for the Navy. In Munk's Roll of the College of Physicians there are in the seventeenth century two instances of surgeons being given the licentiate of the College so that they might administer 'inward' medicines; so this restriction on surgeons persisted into that century. In 1645, Edward Clowes Arris, Alderman and Barber-Surgeon, bequeathed a sum to the Company to found lectures on anatomy on condition that a 'humane' body should once in every year be dissected. In 1655 the Gale Lectures were founded by John Gale, and the two bequests merged into the Arris and Gale Lectures; Havers, who described the Haversian canals in bone, was the first lecturer.

Pepys attended the anatomy lecture and the dinner afterwards in 1662. His inquiring mind, like his master's, Charles II, led him to be interested in

anatomy, and he was consulted as a friend by the Masters of the Company on more than one occasion. Pepys relates that on August 29, 1668, he visited with his friend, Harris, Chirurgeons' Hall, 'where they are building it new, very fine; and there to see their theatre which stood all the fire, and, which was our business, their great picture of Holbein's, thinking to have bought it, by the help of Mr. Pierce, for a little money. I did think to give £200 for it, it being said to be worth £1,000; but it is so spoiled that I have no mind to it, and it is not a pleasant though a good picture'. The Company evidently contemplated selling the picture to help defray the expenses of repairing the Hall, which probably sustained some damage in the fire, but their reserve price was fortunately too high and Pepys did not get his bargain.

Charles II and Queen Anne were both benefactors of the Company. Charles gave them a silver drinking-cup elaborately chased, and Queen Anne a large bowl with a flowered edge.

THE CORPORATION OF SURGEONS

In the eighteenth century, anatomy and surgery made increasing progress. In the royal hospitals, St. Bartholomew's and St. Thomas's, which had survived the Reformation through the representations of the City Fathers, and in the newly founded hospitals like Guy's, the Westminster, St. George's, and others in the provinces, surgeons treated many patients, enlarged their experience of surgical maladies, taught pupils, and were eager to improve their knowledge of anatomy and operative skill by dissecting human bodies. There was growing incompatibility between the barbers and the surgeons, especially in regard to restrictions on human dissections. William Cheselden (1688-1752), the first surgeon and anatomist of his time, as a young surgeon was reprimanded by the Barber-Surgeons for dissecting bodies in his house. At length, mainly through the influence of Cheselden and John Ranby, Serjeant-Surgeon to George II, who had been with that monarch at the Battle of Dettingen in 1743, the Barbers and the Surgeons separated. An Act of Parliament dissolved (from June, 1745) the old union, and enacted that members of the united company who were freemen of it, and admitted and approved surgeons within the rules of the Company, should forthwith be a separate and distinct body Corporate: 'the master, governors and commonalty of the art and science of Surgeons in London'. John Ranby became the first Master of the new Corporation, the constitution of which was mainly that of a City Company. Here again royal sympathy with the ideals and objects of the surgeons can be traced, for no doubt Ranby and Cheselden as surgeons to the king obtained the approval of George II at the outset. The Barbers had the best of the bargain. They retained their Hall, library, plate and endowments. All the surgeons carried with them was the Arris and Gale bequest.

Funds were raised, however, for a new habitation, and in 1751 Surgeons' Hall in the Old Bailey was built from Cheselden's plans (Ottley); he had studied architecture and also designed Putney Bridge. Pennant, in his

'London', observed that by a sort of second sight, 'the Surgeons' Theatre was built near the court of conviction and Newgate'. He added:—

> 'It is a handsome building, ornamented with Ionic pilasters, and with a double flight of steps to the first floor. Beneath is a door for the admission of the bodies of murderers and other felons, who, noxious in their lives, make a sort of reparation to their fellow-creatures by becoming useful after death'.

The bodies of murderers after execution were dissected in the Surgeons' Theatre, according to an Act passed in 1752, and which was only repealed in William IV's reign. Lord Ferrers's body in 1760 was brought here after

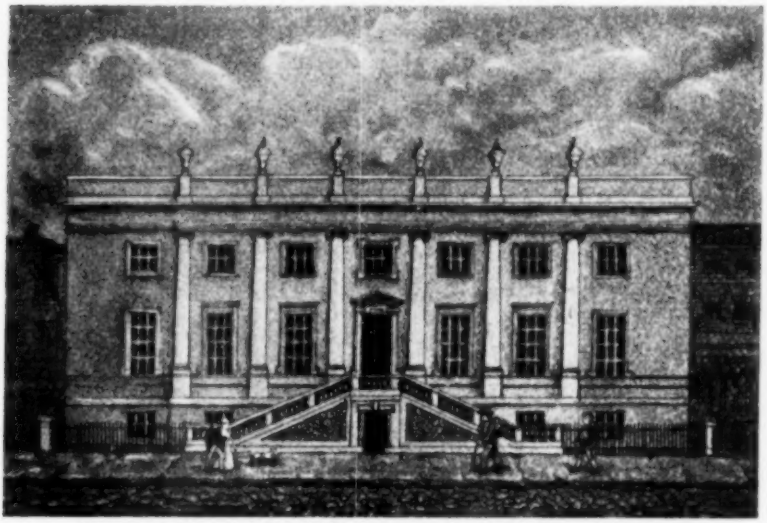

FIG. 3.—Surgeons' Hall, Old Bailey, 1751 to 1796. (*From an old print.*)

he had been hanged for the murder of his steward, but at the request of his aunt, the pious Lady Huntingdon, it was not dissected.

Ten examiners were appointed for the diploma of the newly constituted Company. Part of their duty was to examine surgeons for the Navy and Army as the Barber-Surgeons' Company had done. Dr. Tobias Smollett, the novelist, passed the examination for naval surgeon's mate in 1740, before serving in the Carthagena expedition, and gives a graphic account of the ordeal in 'Roderick Random'. Oliver Goldsmith presented himself in a new suit (not paid for) on December 21, 1758, and was found 'not qualified for ditto'.

Percivall Pott and John Hunter in 1753 were appointed the first Masters in Anatomy. John Hunter's name through his work and the Hunterian Museum is imperishably associated with the Royal College of Surgeons, but he was probably too busy with his scientific researches and 'earning that

damned guinea', to take an active part in administration, although he was a member of the Court of Assistants.

In 1796 the Company of Surgeons abruptly dissolved on a technicality. A Master was elected illegally, a proper quorum not being present. Owing to the opposition of the irascible Lord Thurlow, who detested surgeons, a Bill to legalize the proceedings was thrown out by the Lords after passing the Commons. To add to the troubles of the surgeons they gave up their Hall in this year, and took a house on the south side of Lincoln's Inn Fields on the site of the present building, but could not exercise their proper functions until their constitution was settled. A new Bill for this purpose was rejected by the Lords in 1797.

THE ROYAL COLLEGE OF SURGEONS

The predicament was solved by an appeal to the Crown. On March 22, 1800, the Royal College of Surgeons in London was established by Charter of King George III. The new College at first retained many of the features of a City Company with a Master and Governors, but in 1822, King George IV gave it a supplementary charter which replaced the Master and Governors by a Council with a President and Vice-Presidents. It is interesting to note how several of John Hunter's pupils became famous surgeons and were Presidents of the College. Among them were Sir Everard Home, Bt, F.R.S., his wife's brother and his executor, Henry Cline, F.R.S., John Abernethy, F.R.S., Sir Astley Cooper, Bt, F.R.S., and Sir Anthony Carlisle, F.R.S. These men brought Hunter's science and spirit into the work and teaching of the College.

The importance and facilities of the College were greatly enhanced by the acquisition of Hunter's famous collection. The Government had purchased this for £15,000 in 1799, and the Corporation of Surgeons had agreed to take charge of it. In 1806, the Royal College of Surgeons received from Parliament a grant of £15,000 to build a museum in Lincoln's Inn Fields; three years later a second grant of £12,500 was given; and in addition they spent more than £21,000 of their own money. By the Charter of 1800, they were empowered to examine candidates for the membership (M.R.C.S.), and the examination fees helped them to support this heavy expenditure.

In a letter written to the Company of Surgeons in 1786, John Hunter had urged the formation of a library, but nothing was done until 1800, when the Board of Curators, which managed the Museum, began to collect a library. Its history has been described in W. R. Le Fanu's Vicary Lecture, which traces its evolution through good times and bad to its flourishing position as one of the great medical libraries of the world. Among notable librarians were Dr. Robert Willis, from 1828 to 1845, Mr. John Chatto, from 1853 to 1887, Mr. J. B. Bailey, from 1887 to 1897, and Sir D'Arcy Power, Honorary Librarian.

The Museum and Library, begun in 1806 and finished in 1813, became in

a few years overcrowded with preparations and books; and in 1835-36 the whole building was reconstructed by Sir Charles Barry. In 1847, the College bought Mr. Copeland's premises in Portugal Street, and in 1852 built on them the Eastern Museum. In 1888, the premises were again enlarged; two more museums were added, and the Conservator's house on the eastern side of the building was pulled down, making room for the extension of the Library.

FIG. 4.—John Hunter, by Sir Joshua Reynolds. (*Portrait at the Royal College of Surgeons.*)

William Clift, John Hunter's last secretary, was the first Conservator of the Museum and with Sir Richard Owen (his son-in-law and the famous comparative anatomist), by making preparations, collecting specimens, and preparing catalogues illustrated by beautiful drawings, made the Museum a Mecca of anatomy, pathology and surgery for surgeons all over the world. Their great work has been continued and extended in modern times by Charles Stewart, Sir Arthur Keith, S. G. Shattock, C. F. Beadles, T. W. P. Lawrence, Sir Frank Colyer, John Beattie, Frederic Wood Jones, and others.

At the outbreak of war in 1939, the Museum was closed and the specimens were stored in specially strengthened basements and cellars. These precautions were in vain, for the German air attack on the night of May 10-11, 1941, destroyed a great part of the Museum fabric and specimens. Salvaged preparations were removed to places of safety outside London, but after the war the Museum reopened, and specimens, their reduced number increased by gifts, were restored to the shelves. The statue of John Hunter escaped destruction. The Wellcome Trustees have promised £100,000 to the Restoration Fund, especially for the fabric of the Museum.

Various additions have been made to the buildings of the College in the course of years. Research laboratories have been constructed, and under the Presidency of Lord Webb-Johnson (1941-49) further freeholds were secured in Portugal Street and Lincoln's Inn Fields. These have been equipped as a residential college for postgraduate students and will ultimately become the Nuffield College of Surgical Sciences. With the Royal College of Physicians, the College maintained for many years on the Embankment an

Examination Hall for the Conjoint Diploma (M.R.C.S. and L.R.C.P.) and other diplomas. In 1909, a site was bought in Queen Square where the new Examination Hall of the Examining Board was built. The Imperial Cancer Research Fund's Laboratories were also transferred there, until in 1938 the Fund was incorporated and independent laboratories were built at Mill Hill. There is also the farm for experimental surgical research at Downe in Kent, presented with land to the College by Sir Buckston Browne in 1932. It adjoins the home of Charles Darwin, and Sir Arthur Keith is its Master.

EDUCATION AND EXAMINATIONS

In 1800, the old apprenticeship prevailed and continued well into the

FIG. 5.—The Royal College of Surgeons of England, as it will appear when the Nuffield College of Surgical Sciences is built. (*By permission of the Royal College of Surgeons.*)

nineteenth century. There were no medical schools, and the custom was for the intending student to be apprenticed to an apothecary or surgeon from the age of sixteen, to serve four or more years, and then to study at a London School of anatomy, like the one in Windmill Street established by William Hunter, and 'to walk one of the London hospitals' for a year or more. He then attended at the College of Surgeons and underwent an oral examination of an hour's duration, at the end of which he either passed and received his diploma of M.R.C.S. or was 'referred back to his studies'. The better-off and more ambitious students might become private pupils of a surgeon on the staff of a London hospital, which was an alternative to ordinary apprenticeship. Thus, John Hunter was Cheselden's pupil at Chelsea Hospital as well as attending St. Bartholomew's and St. George's Hospitals; and Benjamin Brodie was Sir Everard Home's pupil at St. George's Hospital. There were no examinations in general subjects, medicine and midwifery, so that a man might be entitled to practise without any knowledge of letters and the greater part of the duties of a general practitioner. As a rule, how-

ever, in addition, most men obtained the licence of the Apothecaries Hall, or, exceptionally, that of the College of Physicians.

Through the exertions of George James Guthrie, a past President, and Sir Benjamin Brodie, President in 1844, a higher order of members of the College, the Fellows, qualified by more advanced age and a higher standard of examination, was set up in 1843. This necessitated a new Charter which was granted by Queen Victoria, the title now being changed to the Royal College of Surgeons of England, certain provincial hospitals being also recognized for purposes of the curriculum. This important reform at once raised the College of Surgeons in status to one of the chief institutions of a great profession, and made it the exemplar of surgical education to the whole kingdom. The Fellowship came to be regarded as the highest surgical distinction in Great Britain, and perhaps in the world. Its regulations were revised in 1900, and again in 1947. The primary part of the examination now includes pathology as well as anatomy and physiology, and both parts can only be taken after qualification.

In accordance with the Medical Act of 1886, the College with the College of Physicians established the conjoint diploma (M.R.C.S., L.R.C.P.). The College, since the days of Sir Astley Cooper and Tomes, has encouraged the study of dental disease, and instituted a dental qualification (L.D.S.) and, subsequently, a Fellowship in dental surgery. Fellowships have also been inaugurated in otorhinolaryngology and ophthalmology, and a Fellowship of the Faculty of Anæsthetists by election. With the College of Physicians special diplomas are granted after examination in the subjects of anæsthetics, child health, industrial health, laryngology and otology, medical radiodiagnosis, medical radiotherapy, ophthalmology, physical medicine, public health, psychological medicine, and tropical medicine and hygiene. In 1909, women were admitted to the College diplomas. The first woman Member was admitted in 1910, and the first Fellow in 1911.

The postgraduate teaching and research activities attract increasing numbers of students, many from the British Commonwealth and from other countries overseas. The bonds of friendship which link the College with the two other Royal Colleges, the Society of Apothecaries, the Royal Society of Medicine, the British Medical Association and other surgical corporations throughout the world have been strengthened, and examinations for the Fellowship are held overseas. The lectures and prizes of the College are famous, in particular the Hunterian Oration and the Jacksonian prize. Research scholarships and fellowships have been founded with great munificence. Since 1947, the *Annals of the Royal College of Surgeons*, a monthly journal under the editorship of Sir Cecil Wakeley, P.R.C.S., have achieved success and popularity, and the *British Journal of Surgery*, under the same distinguished editorship, has its office in the College. The College has, in fact, become a University of Surgery with its own faculties and professors.

The Presidents, who have taken a large share in shaping the destinies of

the College, have been, almost without exception, not only eminent surgeons, but men who by character and influence commanded respect in the outside world. Among these may be mentioned John Abernethy, Sir Astley Cooper, John Hilton, Sir James Paget, Sir John Simon, Sir Jonathan Hutchinson, Sir William MacCormac, Sir Rickman Godlee, Sir George Makins, Sir John Bland-Sutton, and, more recently, Lord Moynihan, Sir Holburt Waring, Sir Cuthbert Wallace, Sir Hugh Lett, Lord Webb-Johnson, and Sir Cecil Wakeley.

CONCLUSION

In the course of centuries, surgery has progressed from a hazardous and limited field, by means of trial and error, experiment and patience, to its wonderful achievements of the present day. The two great advances which live for ever in this continual progress are the discovery of anæsthetics and Lister's work. John Hunter and Benjamin Brodie made surgery a scientific profession, and many have followed in their footsteps: for example, Victor Horsley, Rickman Godlee and Hugh Cairns in cerebral surgery, Moynihan in abdominal surgery, Tudor Edwards in thoracic surgery, and O'Shaughnessy in cardiac surgery. Their scalpels grazed the springs of life and brought healing to the hopeless. Nor should the triumphs of orthopædic and conservative surgery, of Robert Jones, Henry Gauvain and Hey Groves be forgotten, as well as the great work of many surgeons of today.

Consistently, the Crown, from the days when Henry VIII founded the Company of Barber-Surgeons, has helped the growth of surgery by its unfailing support. Her Majesty Queen Elizabeth II by her gracious act in this year of her Coronation has once more encouraged the Royal College of Surgeons in its beneficent work.

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EAR, NOSE AND THROAT EMERGENCIES IN PRACTICE

By WILLIAM McKENZIE, M.B., F.R.C.S.

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When the Health Service began and the system of domiciliary visiting was arranged, we at the Royal National Throat, Nose and Ear Hospital thought that a twenty-four hours' service of trained telephonists would be needed to deal with emergency calls from doctors. To our surprise, very few telephone calls were received at the hospital and none of the consultants has had an emergency call oftener than once a fortnight. This is a great change compared with the years before the war, when emergency calls were to be expected two or three times a week. The main reason is, of course, penicillin, which controls nearly all the acute infections in our specialty. The other reason, a more doubtful one, is that the general population looks after itself better. Before the war, a new case of brain abscess was to be expected two or three times a month. These nearly always followed a chronic ear discharge, and neglect of the ear led to the disaster of intracranial infection. Nowadays, brain abscess is seldom seen, although chronic ear infection seems to be as common as ever. Perhaps chronic suppurative otitis media is seen earlier; certainly the younger otologist is prepared to deal with it before symptoms of spread arise. The latter may be the true reason, combined with the power of penicillin to deal with any infection which is due to sensitive bacteria.

In compiling a list of emergencies which are still encountered, it is difficult to be precise in deciding what the word emergency means. It is really a combination of two things: the emergency in the mind of the family doctor and the emergency as the specialist understands it. It is idle to say that these two ought to be the same, for the specialist does nothing but think of his own small field, and has been trained to do so, whereas the family doctor has to recognize urgent disease in any part of the body. An example of this is as follows:—

> A neurologist referred to me a man of forty with a facial paralysis on the same side as a discharging ear. I had no difficulty in recognizing a paralysis of the facial nerve due to a long-standing cholesteatoma, and I explored the ear on the same day. Four weeks after operation his face was recovering. The neurologist, a registrar of several years' experience, sent this case to me with a diagnosis of Bell's palsy and discharging ear. That a trained observer could make such a misleading diagnosis goes far to explain the difficulty which the family doctor might meet in the same situation.

ACUTE OTITIS MEDIA

Acute otitis media still takes first place as an emergency. Anyone who has nursed a sick child with earache through the night is unlikely to forget the

experience, but the edge has fortunately been blunted by penicillin. Since the introduction of penicillin, I have not seen one child with a painful otitis media who has not been relieved within a few hours. The penicillin must be given properly, however, and this means injections. I still see children who are treated with penicillin by mouth and even by eardrops, with, of course, no effect. The reluctance to use a needle is easily understood, and after many conversations with general practitioners, I realize that their cases of otitis media are not quite the same as mine, for my cases are later and more acute.

A reasonable compromise, in a child at all events, is to try a sedative and some warm ear drops for a few hours if the temperature is not high. If this treatment is not a success, or if the general condition makes such mild measures unwise, then penicillin should be given at once and in full doses. No one need fear masking of symptoms in penicillin treatment. Penicillin can in fact be given at any stage in an acute otitis media without fear of masking.

I prefer to admit a child to hospital if penicillin is needed for an acute otitis media, for the injections can be given more easily and more often than at home. In this way, the usual dose is 50,000 units of penicillin four-hourly; procaine penicillin in aqueous suspension (e.g. 'distaquaine'), given once daily in large doses such as 300,000 units, also produces excellent results.

Acute influenzal otitis media.—A patient who is ill in bed with influenza, suddenly develops severe pain in one ear. There is no discharge, and only slight deafness, and the auriscope shows the typical red blisters scattered about the meatus and drum. The temperature is only slightly raised. This is the usual appearance of an influenzal otitis. It is an emergency because of the acute pain and because the patient cannot be moved as he is already in bed with influenza. The pain seldom lasts more than a few hours, and the infection clears up quickly by itself, which is fortunate, because penicillin injections have no effect.

My practice is to advise a strong sedative such as morphine, $\frac{1}{4}$ grain (16 mg.), but to avoid penicillin unless a secondary infection causes the ear to discharge.

Myringotomy.—This article has really been inspired by a recent discussion of myringotomy in otitis media. The coming of penicillin has altered the practice of this specialty so profoundly that few experienced otologists have been able to adjust themselves to it. The operation of myringotomy is a good example of this difficulty. Before the advent of penicillin there was general agreement that an early myringotomy relieved pain but that it did not prevent a mastoid infection. Furthermore, if a myringotomy was necessary, the infection was severe and the patient should be admitted to hospital. Since the introduction of penicillin, the value of myringotomy at any time is in doubt. Some say that myringotomy must be done to promote resolution of the infection and to avoid deafness afterwards.

I can only reply to this that I have not advised a myringotomy for the last four years. My patients have had large doses of penicillin at once, with a note that if the earache lasts overnight a myringotomy should be done. It has never been necessary, nor have my patients suffered from permanent deafness afterwards.

ACUTE MASTOIDITIS

This is not an emergency, but the idea dies hard in every practitioner's mind. It has never really been an emergency, for I was taught as a student that there was no case of mastoiditis which could not be watched for twenty-four hours, and that was before the days of the sulphonamides. It has often been said that the whole middle ear cleft is involved in an acute infection, so that every case of otitis media involves the mastoid cells as well as the middle ear. To most otologists of my generation, however, the term acute mastoiditis is rather loosely applied to a case in which a mastoid operation is contemplated for acute otitis media. This definition held good in the days before penicillin, but it means little now, for every case of this kind should be tried with penicillin. The experience of Moffett in Birmingham, and of McGuckin in Newcastle, shows that penicillin will clear up even a subperiosteal abscess secondary to a mastoiditis, and that incision of the abscess is unnecessary. Few otologists will go as far as this (perhaps because they cannot adjust themselves fully to the value of penicillin), and I usually advise that the abscess should be incised and drained while penicillin is given at the same time.

Acute mastoiditis and meningitis.—This is best discussed by a recent example:—

A month ago I was called urgently to see a boy of five. He had complained of earache for twelve hours and his temperature was 103° F. (39.4° C.). When I examined him, I found the right drum bulging and bright red. There was no discharge, but the child had marked neck rigidity, which suggested meningitis. He was admitted to hospital, and after treatment with penicillin injections lost all his symptoms within forty-eight hours. He was discharged after seven days.

It is true that this child recovered after treatment which could have been given in his own home, but I doubt whether anyone would contradict the suggestion that a patient with a serious complication of otitis media is better nursed in hospital. It is true, too, that the child recovered with penicillin injections and nothing else, but it seems unfair to add a difficult case of this sort to the responsibilities of a family doctor.

Twelve months ago I was asked to see a patient in a medical ward. She was a woman of forty who had been admitted seven days before with severe vertigo and a high temperature. The notes were not very full, but the woman told me she had suffered from earache at the beginning of her illness although she had never before had trouble with her ears. She had been treated with large doses of intramuscular penicillin on admission to hospital and the temperature had fallen to normal in three days. When I examined her I found the right ear completely deaf, and later when I was able to test the vestibular nerve, I found it quite inactive.

This story can, I think, be interpreted as follows: the patient was admitted to hospital with a severe infection of the middle and inner ear; the invading organism was sensitive to penicillin and in consequence the patient's life was saved, although the ear was already destroyed by the disease. She was therefore cured by penicillin without an otologist's help.

These cases were not uncommon before the discovery of penicillin. They led to meningitis and death, and the surgeon seldom had a chance to do anything. Penicillin will now cure this kind of infection, and however useful the otologist may be in making a precise diagnosis, the fact remains that he is no longer needed as a surgeon.

OBSTRUCTION TO THE EUSTACHIAN TUBE

This is a new emergency in our specialty; the condition has been well known for many years, but as an acute condition it is peculiar to air travel. It is felt on descent in an aircraft and is due to the unequal pressure between the middle ear and outer air. Its forerunner is often a cold or some infection which hinders the normal action of the Eustachian tube orifice in the naso-pharynx. The condition has a number of names, all difficult to remember, and is called 'otitic barotrauma' in the R.A.F.

The best *treatment* is to do nothing and await the natural recovery, which is certain but takes time. Inhalations can be given as a palliative in the interval of waiting. Catheterization and inflation of the Eustachian tube may relieve the condition for a few days, and if it is already improving may lead to complete recovery. The difficulty is to know what stage the obstruction has reached; gentle inflation of the Eustachian tube does no harm, but no promise can be made that it will cure the obstruction at once. I have been asked to see about two cases each year since the war as emergencies, but this is probably because I see patients for one of the airlines.

CHRONIC SUPPURATIVE OTITIS MEDIA

An emergency due to chronic ear suppuration is now rare, although patients with this complaint form a large part of an out-patient clinic. Penicillin will control a spreading infection from a chronic otitis media, but it has no effect on the ear itself. This may perhaps account for the small number of urgent calls to the otologist, for the family doctor will naturally give penicillin himself if he thinks the infection is spreading from an ear.

The only complications which the otologist sees regularly are vertigo and facial paralysis. Neither is so urgent that he is called out at midnight, and I have only been called once in the last four years to see a case of facial paralysis as an emergency.

MÉNIÈRE'S DISEASE

The otologist considers that patients suffering from Ménière's disease should attend his clinic for treatment and not that of the neurologist, but however correct this may be, the neurologist is usually asked to see a patient

in an acute attack, not the otologist. The reason for this is probably that the vertigo is obvious and conceals the deafness.

A friend of mine telephoned me one evening and asked me to visit him urgently as he was giddy and violently sick. I found him curled up in bed with his eyes tightly closed and his left ear uppermost. When I succeeded in opening his eyes he had a second degree nystagmus to the right, and I found the left ear very deaf. He recovered in three weeks and examination later confirmed the diagnosis of Ménière's disease.

THE NOSE

The most common emergency is, of course, epistaxis. It is more annoying than dangerous, and every general practitioner must have had the experience of being called out in the middle of the night to a patient who has had an epistaxis, but has only lost a small amount of blood. In a mild case, the best course is to ask the patient simply to hold the nostrils together with his fingers for ten minutes by the clock. If this fails he should be put to bed and given enough sedative to keep him drowsy. I usually order 1½ grains (0.1 g.) of 'seconal', to be repeated if required. The sedative usually controls the bleeding, and the nose should only be packed if it fails. The family doctor is wise to ask the help of a specialist to pack the nose, for this is a complicated procedure to do properly, and needs a cocaine spray, a headlight and a nasal speculum. I still find, however, that I am called to see a patient with epistaxis whose nose has already been packed, but for whom no sedative has been ordered.

Six months ago I was asked to see an old man of eighty who had been admitted to hospital for epistaxis. The surgeon on duty had been most attentive; he had fitted up a blood transfusion and had given the old man altogether four pints (2 litres) of blood; he had also packed the nose. When I saw him, I was struck by his wakeful behaviour; he coughed and spat constantly, looking at his handkerchief for streaks of blood. When I asked about a sedative, I was told that none had been given. I ordered morphine, ¼ grain (16 mg.), to be given and repeated when necessary, and removed the nasal pack. He did not bleed again.

A warning should be given about the nasal pack: it should never be left in place for longer than forty-eight hours, for it becomes infected after that time and may produce an acute otitis media.

A few months ago I was called to see a child of eight in a poor quarter of London. She was in bed with measles, and her nose had bled on and off for two days, although she had not lost much blood. When I examined her, the bleeding had clearly come from the right side of the septum. She would not allow me to spray her nose with cocaine, so I could do not more than reassure the parents. This case defeated me, but fortunately she did not bleed again. The only solution would have been to admit the child to a fever hospital, where she could have been treated with sedatives.

ACUTE SINUSITIS

Most doctors treat an acute sinus infection themselves and do not call in a specialist. The rules of treatment are indeed well known, and specialist treatment is seldom required at first. The patient should be nursed in bed,

and given sedatives and frequent inhalations, and penicillin injections if the temperature is high.

Occasionally, however, a patient is referred as an emergency with an acute frontal sinus infection. Our practice is to treat this by nursing in bed as for any acute infection, and when the temperature falls to normal, to puncture and wash out the antrum on the affected side, if the x-ray suggests infection. No more elaborate operation is required, and operation on the frontal sinus itself is now unusual and reserved for chronic infection.

The following is an example of the power of penicillin in an acute infection of the frontal sinus:—

I was asked to see a man of forty who was acutely ill. He had a temperature of 104° F. (40° C.) and was unconscious and apparently moribund. The only sign was tenderness and slight œdema over the frontal sinus. I advised that he should be admitted at once to hospital for penicillin treatment, but warned the relatives that the prognosis was poor. To my surprise, two days later the house surgeon told me that the patient was sitting up in bed asking for his breakfast. He recovered completely after a month's treatment.

ACUTE TONSILLITIS: QUINSY

In the last four years I have only been called twice to see a case of acute tonsillitis as an emergency. In both cases the practitioner thought the infection was due to diphtheria and wanted my support to recommend admission to a fever hospital. I agreed with the diagnosis each time, only to be contradicted by the pathologist.

The first case occurred in a girl of eighteen, whom I saw on a Saturday morning. She was not ill, but one tonsil was covered with a thick grey slough. The temperature was 99° F. (37.2° C.). The report on the throat swab was not available. I advised that the infection should be considered as diphtheria and that she should be transferred to a fever hospital at once and given antitoxin. The throat showed a pure growth of *B. friedländer*. The girl recovered in a few days.

Quinsy: Peritonsillar abscess.—Even before the discovery of penicillin, a peritonsillar abscess needing incision was seldom seen. It usually occurred in patients who neglected themselves, and who came late to the doctor's surgery. The specialist was, in fact, seldom asked to do anything and now only one or two cases of quinsy come for treatment in a year.

Penicillin is a powerful drug in quinsy and if given early will make incision unnecessary. Even in an advanced infection, twenty-four hours' penicillin treatment may be enough to avoid the need for surgery.

The general experience for many years has been that it is wise to delay incision for a quinsy until it is certain that there is pus and that the pus is close to the surface of the mucous membrane. Every surgeon has had the experience of plunging about with a knife and sinus forceps around a tonsil and finding nothing but blood; and to have had this experience once is enough to make one cautious when faced with a quinsy of any kind, however obvious the swelling may appear. In fact, penicillin injections may now

be recommended in every case, and nothing will be lost by postponing incision for a few hours.

TRACHEAL OBSTRUCTION

A new growth in the larynx or upper trachea may cause an acute obstruction. It is an uncommon emergency, although I have seen two cases since the war. The points to remember are that stridor first occurs at night or at meals, and that cyanosis is a late and dangerous sign.

A new growth of the larynx begins, of course, with hoarseness, and obstruction is late, but carcinoma of the trachea does not cause hoarseness.

A practitioner in the home counties telephoned me one night about a patient who had all the signs of laryngeal obstruction with severe inspiratory stridor, but there was no hoarseness and the voice was good. The practitioner thought this was an unusual combination and so did I, but the laryngeal mirror explained it at once. The obstruction was due to carcinoma of the trachea. In spite of deep x-ray treatment the patient died within twelve months.

FOREIGN BODIES

Foreign bodies in the œsophagus are a nuisance to everyone, because it is seldom possible to be sure whether the pain and dysphagia are due to the foreign body itself or to a tear made by its passage. An x-ray will help, and so will the patient's behaviour. Dysphagia which is improving usually means that the foreign body has passed on; dysphagia for solids but not for fluids in the first twenty-four hours will allow the patient to be watched, for œsophagoscopy is then not urgent. Actually, most œsophagoscopies for a foreign body show nothing.

A foreign body in the trachea or bronchi is serious and should be regarded from the first as an emergency. The patient is often a small child and if the foreign body is of vegetable matter, such as a walnut, the condition may be quickly fatal. Although everyone knows of the dangers, a foreign body in the trachea or bronchi is so rare that one specialist is only likely to see three or four in his lifetime. Removal of the foreign body needs special skill and instruments, and it is to be hoped that one day a centre will be established to serve the whole of England, to which patients may be sent by air.

CONCLUSION

This account has been written from the experience of one specialist in London since the war. Although at least half a million people live in the area served, the telephone seldom rings out of hours, so that this specialty now offers a quiet time to those who practise it, when they have finished the ordinary busy out-patient clinics.

THE SHIP-SURGEON'S LIFE

By JOHN S. MEIGHAN, M.B., Ch.B., B.Sc.

In the eyes of the public the life of a ship-surgeon is commonly invested with glamorous and pleasurable surroundings and circumstances of all sorts. He is supposed to recline on a bed of roses, when he is not sporting with Amaryllis in the shade, or with the tangles of Neaera's hair. It is the purpose of this article, which is based upon twenty years' experience as a ship-surgeon, in both the Merchant Navy and the Royal Navy, to 'debunk' (as far as possible) this quite unfounded conception.

The position of ship-surgeon has not always held, in the eyes of the public, the glamorous attraction it appears to do at present. In days gone by, when medical service on board was most primitive, when the surgeon was paid something like £5 per month, and had to bring his instruments with him, and when, in consequence, the dregs of the medical profession drifted out to sea, the old-time ship-surgeon, rarely sober, whose main duty on board seems to have been that of ship's jester and entertainer, created for himself an ugly reputation which has, even to present times, left a nasty taste in the mouth of the travelling public. Nowadays, however, when conditions of equipment and pay are so much better, the status of the ship-surgeon has correspondingly improved; the old-timers have been eliminated (where, indeed, they did not eliminate themselves by their habits); and it may be taken as certain that no important shipping company would employ as surgeons any but reputable and experienced medical men, who are required to give unexceptionable references as to character.

THE LEGAL ASPECT

The legal position is that if the total number of persons, i.e., crew and passengers together, on board a ship proceeding overseas, is, or exceeds, 100, a surgeon must be carried. This means that it is the exception, rather than the rule, for an overseas-voyaging ship to have a surgeon on board. The Port Medical Officer of one of our busiest ports recently told me that about one ship in every ten carries a doctor. Occasionally, in the interests of passengers, a more generous-minded shipping company will put a surgeon on board a ship with rather less than the above number.

THE SHIP WITHOUT A DOCTOR

In the case of a ship without a doctor the responsibility for dealing with serious illness while the ship is on the high seas lies in the hands of the Captain. To help him in dealing with such a situation the Captain is provided with an excellent handbook, 'The Ship-Captain's Medical Guide' issued by the Ministry of Transport. Then, there is medical consultation by

wireless with ships carrying a doctor, and for which special codes have been arranged by the Ministry of Transport. Thirdly, in the event of major surgical conditions, transfer of the patient to the nearest ship with a surgeon on board is possible, subject, of course, to weather conditions. I have myself participated many times in the two latter expedients, the first of which (consultation by wireless) is always a difficult matter for both parties.

THE WORK OF A SHIP-SURGEON

No matter how healthy and satisfactory their circumstances and surroundings may be, people are always liable, on occasion, to sudden illness. Cases of acute appendicitis occur now and then in Swiss hotels and other places ideal from a health point of view. The same holds good in the case of ships, however modern and hygienic; indeed, even more so, considering the sudden changes of climate to which all on board are subject during a voyage of any duration, also the dietetic risks taken ashore at various ports of call. To this must be added: (1) the almost invariable presence on board, among the passengers, of cases of chronic illness, e.g. diabetes mellitus, gout, arthritis; (2) the presence on board of the crew, who are 'super-liable' to accidents, right round the clock. Passengers seem strangely oblivious of the latter; they mostly have the idea that the doctor is on board primarily in *their* interests, whereas, strange as it may seem, in strict legality, there is no onus on the shipowner to provide a surgeon for passengers *per se*—except in respect of an old-standing legal requirement whereby a doctor has to be provided when 50 or more emigrant or third-class passengers are on board. I am regularly asked by passengers whether I 'go up country' at terminal ports: they never seem to realize that it is just when the ship is working cargo in port that accidents are most liable to happen, and the doctor, in consequence, most likely to be needed.

Everything, of course, depends upon the size of ship, and therefore of her complement. There is a vast difference between the small 'passenger-cargo' ship with just over 100 'souls on board' and the large modern passenger-liner. The two Cunarder 'Queens' have each, when full, a total complement of round about 5000 persons on board, to meet the medical needs of whom two surgeons, 3 nursing sisters, and six hospital or surgery attendants are required. I have myself served in a ship which had, in addition to myself, an assistant surgeon, two nursing sisters and two attendants. In these large ships, with their relatively huge complements (equivalent, in the Cunarders mentioned, to the population of a medium-sized town) *any* sort of emergency may arise at *any* hour, from which it follows that the surgeons on board have to be 'universal' specialists, of a sort able to give at least first aid in the various specialties, and, in any case, capable of doing a 'straight' appendix, closing a perforated peptic ulcer, and relieving an intestinal obstruction. To these duties must be added the ordinary everyday run of minor maladies, much the same as one finds in general practice ashore, plus various other

duties of a quasi-professional nature. It is therefore scarcely necessary to say that in large ships the surgeon's job is no sinecure.

Unfortunately, in the past at least, there has been a tendency on the part of newly qualified practitioners to look upon a voyage or two as a ship-surgeon as the right thing to do upon qualification, partly as a restful holiday (free of charge—indeed paid) after the strain of the final examinations, and partly as a means of 'seeing the world' before settling down.* Anyone with such an idea in respect of shipping companies like the Cunard, P. & O., Orient, Union-Castle, Royal Mail, to mention a few, should drop it *statim*. In the first place, as already pointed out, the large ships of these companies are no place for the holiday-seeker, and in the second, the managers of these lines just don't *want* men of this sort. They look, naturally, for mature, experienced practitioners prepared to stay with them, not just for a voyage or two, but for years, making the sea their career. Indeed, in view of this, one or two of these companies have pension schemes for their surgeons as well as for their other officers.

THE SEA AS A CAREER FOR THE DOCTOR

A man may have some minor degree of physical incapacity which makes general practice (especially these days!) too great a strain on his health, and at the same time may not have the means or ability to enter the fierce competition of the specialties. At sea, his work is all round his doors, and he never has to travel farther than one or other end of the ship. He is relieved of many minor responsibilities, and has no overhead expenses (all shipping companies now provide a full range of medicines, instruments, and equipment, some on a lavish scale). In his ship's home port, he has regular leave, the length depending upon the length of voyage, during which he does not need to provide a deputy. Here let it be noted that at sea one stands right outside the National Health Service as soon as the ship has left its home port. While in the home port, officers and crew are medically taken care of under the National Health Service.

Again, there may be that inherent love of the sea, which is so widespread among the inhabitants of these Islands, to which may be added the attraction of moving about the world, constantly meeting new people of all types, and occasionally coming into professional contact with persons whom one would never encounter in the average shore-doctor's life. During my own sea-going life, for instance, I have had various distinguished personages, in-

*I have often felt that the distinguished London surgeon, Mr. J. Johnston Abraham, C.B.E., D.S.O., F.R.C.S., has been to some extent responsible for this attitude in view of the popularity of his excellent book, 'The Surgeon's Log', written in the early 1900's and describing his experiences during a voyage to the Far East in a Blue Funnel liner (now available in the 'Penguin' series). A recent and very popular book, Dr. Richard Gordon's 'Doctor at Sea', is largely written in semi-humorous vein, and obviously pertains to the small 'passenger-cargo' type of ship mentioned above.

cluding a few of the minor Royalties, and some Cabinet Ministers, as patients.

Another advantage, which, as a rather selfish one, I hesitate to bring forward, is that the 'chronics' automatically disappear at the end of each voyage. On the other hand, there is the disadvantage that, with rare exceptions, it is not possible to follow one's cases right through to their termination, if the illness is at all serious.

Another drawback is that, except in the largest ships, financial earnings are lower than ashore. Pay is certainly higher now than it used to be, and in all passenger-carrying ships the surgeon is allowed to charge fees—from 5*s*. to 10*s*. per attendance or visit according to class, including all medicines or other forms of treatment—for attendance on any illness not in any way connected with the ship (this, incidentally, is occasionally a somewhat difficult matter to decide). Accidents on board are normally treated free of charge,* and, of course, in all cases the officers and crew are treated free. Even so, however, one can never hope to reach the figures made by the large-practice general practitioner or specialist ashore.

Again, there is the breaking of family life if one is married, a serious feature in long voyages. Whereas the wife of the naval medical officer can make a home for him in any part of the world (even when he is sent to China in a cruiser for three or more years), the Merchant Navy surgeon's wife has practically always to live in the United Kingdom.

A small advantage of a material sort, which might be mentioned, is that, at present, one lives *very* much better afloat than ashore; rationing *does* apply to ships, but only in 'bulk', and the menus of the higher-class lines approximate to those of peace-time. In addition, one is allowed to bring into the United Kingdom from abroad a moderately large amount of foodstuffs, free of duty, provided these are for strictly domestic consumption.

I believe that I am correct in saying that surgeons of the 'West End' type, about to retire, often consider taking up work as ship-surgeons. Whilst, *qua* major surgery, this would be an ideal job for them, they should remember that a ship-surgeon has many many things to do on board beyond major surgery; indeed, on the whole, the latter is rare. In addition to being a 'G.P.' afloat, he has to perform the hundred-and-one petty duties attaching to this type of work, only too well known to his confrère ashore. As well as this, he has many things to do of a *quasi*-medical nature, e.g. trying, in company with his closest colleague on board, the Chief Purser, to persuade the elderly, neurotic lady, full of ailments (not serious enough, of course, to justify calling the surgeon when the latter's services are not free) to give up the lower berth she has wrongly occupied, and return to her rightful one, the upper. Instances of this kind could be quoted *ad nauseam*—any experienced

*I have always considered it only fair that passengers whose injuries are the result of 'playing the giddy goat' should pay for any treatment that may be required for the results of their escapades.

traveller will understand. To all this must be added the care of venereal disease, in all its forms and stages, among crew and, occasionally, passengers. I may be wrong, of course, but somehow I cannot see the surgical specialist settling down happily to these multifarious duties, to which he has long become unaccustomed.

THE MERCHANT NAVY *vs.* THE ROYAL NAVY

What advantages, if any, does service as surgeon in the Merchant Navy have over service in the Medical Department of the Royal Navy? This is rather a difficult question to answer, as so much depends upon one's tastes and desires. So far as prospects, pay and pension are concerned the Royal Navy is definitely better, but the Merchant Navy surgeon has a much more regular and settled life. He is not at all likely to be sent, at forty-eight hours' notice, like his confrère, to some outlandish place in the world for three or more years. Again, even allowing for 'Wrens' and the wives and families of 'dockyard maties', the Royal Navy surgeon does not have the continuous contact with women's and children's troubles that the Merchant Navy surgeon does; from which it follows that the latter can step ashore at any time into general practice in a way that the former usually cannot. Moreover, the male part of the Royal Navy surgeon's practice, which means usually, the *entire* part, has been medically 'screened' to a degree to which the motley collection largely comprising the Merchant Navy personnel these days has not and, indeed, cannot be, despite the efforts of the conscientious medical officers of the Shipping Federation. The result is that, apart from venereal diseases, dermatology and infectious diseases, nearly all his cases are acute emergencies and accidents.

CONCLUSION

I shall bring this brief account to a close by a long quotation from the work of one whom, in his own specialty (if one can so call it), Osler would have called 'a master in Israel'—the late Dr. A. Vavasour Elder's 'The Ship Surgeon's Handbook'.*

> 'Rightly or wrongly, as a rule the general travelling public, and also the medical profession, appear to have little faith or confidence in the sea-going practitioner. If he be a young man fresh from medical school, then he can have had no practical experience—where does the newly qualified man get his clinical experience elsewhere but among the public? Should he be advanced in years, his presence on board is generally attributed to either drink, drugs, debility, or to some professional or domestic debacle! On this subject nothing further need be said, beyond stating that a medico at sea will always be treated according to his own merits and behaviour . . .
>
> 'The modern liner, with her population verging near or over four figures, bound on a voyage of five or six weeks' duration, with several ports of call—usually a

*Published by Baillière, Tindall & Cox, latest edition 1926. As will be understood, though the general advice in the book remains invaluable, the therapeutic part is naturally now out of date.

fruitful source of work for the doctor—affords plenty of scope for a medical man, both at sea and in port . . .

'To most minds, lay and medical, the life of a doctor on board appears to be light and easy. He has all night in his bunk—presumably—and is protected from the vagaries of the elements by having no "watch" to keep. His public performances consist mainly in appearing at the gangway when passengers are embarking, or to receive local health authorities when the ship enters port and obtain *pratique*;* a daily attendance at the surgery at stated hours, to dole out measures of black draught or other aperients; to preside at a table in the saloon, and then his day's work is done.

'No thought is ever given by the travelling public to his responsibilities, medical and moral, in dealing with an epidemic disease which may, perhaps, attack the whole ship; his anxiety in a case of enteric fever or pneumonia, where careful nursing, almost the whole essence of treatment, is practically unobtainable unless a trained nurse happens to be among the passengers, and volunteers her services; his doubts in a case of probable malingering, knowing full well that if he makes a mistake in either direction his reputation among the crew is gone; the decision as to the exact point at which a slightly sick man must be laid off duty—all these are unknown and unseen, consequently unappreciated.

'He is in a position of splendid isolation, having no one on board in sympathy with his work. In fact, the very exercise of his duty at times antagonizes all other departments in so far as their own work is concerned. Moreover, none of these will share any blame attaching to the results of his attempts to satisfy everybody . . .

'A ship-surgeon lives on possibilities. The whole gamut of medicine, surgery, and midwifery lies within his sphere, and may arise at any moment calling for prompt measures. The following record of a day's work while taking 1,600 emigrants to Australia may be of interest. It included one normal labour, a compound fracture of tibia and a dislocation of shoulder (the weather was bad at the time), three dental extractions, four abscesses incised, in addition to routine surgery hours, and with diphtheria and scarlet fever both prevalent in epidemic form. This is not quoted as being typical of an ordinary day's work at sea, but more as illustrating the various possibilities at any given moment . . .

'All these little items, with others too numerous and trivial to mention, which in some instances constitute more worry than work, tend to make the surgeon's position in a large liner anything but the bed of roses most people imagine it to be. However, as a training in self-reliance, decisiveness of action, tact and good management, it is equalled by few and surpassed by none of the earlier stages of a medical career. A year or two in a large ocean liner before commencing practice is by no means waste of time, and need never be a source of regret to the man who launches into professional life in this fashion'.

In perusing the above, the reader should bear in mind the fact that it was written in the early 1900's, but in my opinion, the views and advice given still hold good today.

*Permission to enter port and disembark or embark passengers and/or cargo.

COBALT 60 BEAM THERAPY UNIT

By B. W. WINDEYER, M.B., F.R.C.S., D.M.R.E., F.F.R.

Professor of Radiology, University of London; Director, Meyerstein Institute of Radiotherapy, Middlesex Hospital.

At a special meeting of the British Empire Cancer Campaign on March 10, the President, H.R.H. The Duke of Gloucester, announced the gift of a Cobalt 60 beam therapy unit from Canada. The gift was inspired by Canadian workers in the field of cancer and radiotherapy with the help and sympathy of Mr. Paul Martin, the Canadian Minister for Health and National Welfare. It was made possible by the generosity of Mr. J. McConnell of Montreal, a noted philanthropist and Chairman of the Royal Victoria Hospital, Montreal, who has paid for the entire unit at a cost of more than £25,000. British radiotherapists and physicists have thus been given an early opportunity of

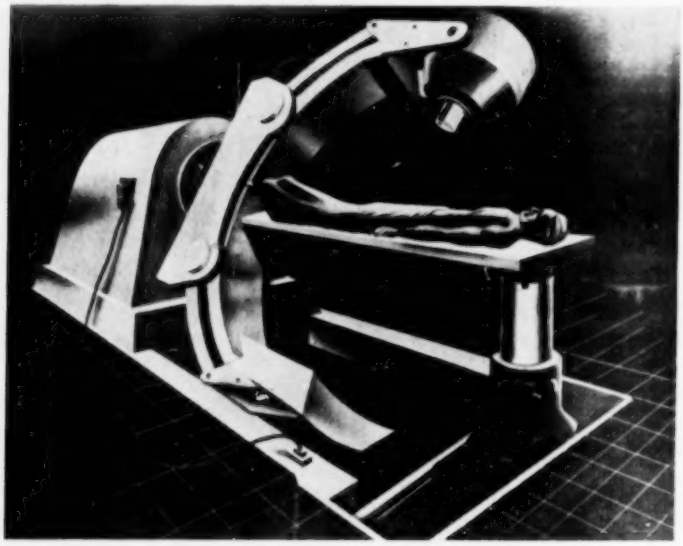

Fig. 1.—Cobalt 60 beam therapy unit.

participating in research into the clinical possibilities of this latest and most powerful development in the use of radioactive substances.

THE DEVELOPMENT OF THE UNIT

Cobalt 60 is a radioactive isotope which is produced by the exposure of cobalt to a heavy neutron flux in the nuclear reactor or atomic pile. It emits a practically monochromatic beam of gamma rays which has somewhat greater powers of penetration into tissues than that from radium. It has been used

as a substitute for radium needles and tubes in various methods of clinical application and has also been used to replace radium in some of the existing teleradium units in this country. Cobalt 60 has an advantage in that it can be obtained with a high specific activity of radiation, i.e., a vast amount of energy in a small volume of metal, and it has been possible to load as much as 50 curies, the equivalent of over 60 grammes of radium, into apparatus constructed as 10-gramme radium units.

The Canadian atomic pile at Chalk River with a high rate of neutron flux is capable of producing Cobalt 60 in considerable quantity with a higher specific activity than has so far been obtainable and the idea of using this to construct massive beam units equivalent to supervoltage x-ray apparatus was conceived by the engineers and physicists of Atomic Energy Limited of Canada, a Canadian Crown Corporation. With the collaboration of the staff of the National Research Council of Canada they developed a unit containing 1,100 curies, the equivalent of about 1,500 grams of radium.

The first unit was installed in November 1951 in the Victoria Hospital, London, Ontario, and about the same time another unit, with the same amount of Cobalt 60, also activated at Chalk River, but designed and constructed by H. E. Johns and the staff of the University of Saskatchewan, was completed at Saskatoon. These units have been continually in use for the treatment of patients since then, and more recently a third one has started work in Vancouver.

As the result of the experience gained by the first units a new model has been designed and it is one of the first of these which has been given to the British Empire Cancer Campaign. It will be demonstrated at the Seventh International Congress of Radiology in Copenhagen and then delivered to Mount Vernon Hospital, Northwood, for clinical research work.

CLINICAL APPLICATION

The beam of radiation coming from the unit can be compared in penetration power in tissues to that produced by an x-ray machine working at three million volts. It delivers a dose rate of 25 roentgens a minute on the skin with a source to skin distance of 1 metre, and over fifty per cent. of the dose delivered on the skin will be received at a depth of 10 centimetres in the tissues. It is therefore possible, with an arrangement of a small number of converging beams, to give high dosage to any deep-seated tumour, in any situation in the body, without causing heavy irradiation of the overlying normal tissues. The unit is also designed so that, if desired, rotational therapy can be carried out. The lead container for the Cobalt 60 is mounted on one end of a gantry and can be rotated around the patient during treatment, the beam of radiation being constantly directed to the tumour throughout the exposure. The position of the patient, on a couch with hydraulic control of movement, can be adjusted so that the tumour site is in the centre of the axis of rotation. A lead counterweight at the other end of the gantry acts as

an absorber of the primary beam and thus reduces the problem of protection of the walls of the treatment room.

The beam of radiation is shut off by a lead screen with remote control except during the actual period of treatment and the whole unit is adequately protected for safe handling during positioning of the patient. It has been possible to solve the protection problem of this unit of such vast power without its becoming too massive and unwieldy because of the small size of the cobalt source which is in the shape of a disc 1 inch in diameter and half an inch thick. On technical as well as economic grounds it would not be possible to construct such a unit with radium of equivalent power, as the radium would take up too great a space and would need a much larger and heavier protective container. Even if such an amount of radium could be made available the cost would be prohibitive, being in the region of £3,000,000.

One of the most attractive features of the development of these large beam therapy units with radioactive isotopes is that a source of high energy radiation is made available, convenient for clinical use and without the complication of high-voltage electrical apparatus. It has a known constancy of output, no risk of major breakdown, few expendable parts and relatively low maintenance costs. There is, however, the disadvantage that the source decreases in strength at a definite rate depending upon the half-life period of the isotope being used. With Cobalt 60 the half-life period is approximately 5 years, and it is therefore necessary to use dose calibration charts making allowance at regular intervals for decreased intensity and to arrange for the reactivation of the cobalt source in an atomic pile after three or four years.

THE FUTURE OF HIGH-ENERGY RADIATION

The development of high-energy radiation apparatus has gone on apace during the last ten years. Clinical and radiobiological research is now being carried out in this country with various types of apparatus, not only in the one to four million volt range but with machines working up to 30 million volts. In the United States even higher voltage machines have been developed and used for experimental purposes.

Fundamental biological research work in the range of voltage in excess of four or five million is only just beginning and no assessment of its clinical value can yet be made, but a considerable amount of clinical experience is accumulating in the one to four million volt range. It has been shown to have definite advantages in the treatment of certain deep-seated tumours. This generous gift from Canada is particularly welcome as it will give an opportunity for comparison in this country of the clinical possibilities of this Cobalt 60 source with those of the two million volt Van de Graaf machines already working and the linear accelerators of four and ten million volts soon to be installed in several centres.

CURRENT THERAPEUTICS

LXV—ANALGESIC DRUGS

By C. A. KEELE, M.D., F.R.C.P.

Professor of Pharmacology and Therapeutics, University of London, Middlesex Hospital Medical School.

Drugs can relieve pain in many ways. Spasmolytics may help by relaxing certain types of smooth muscle: for example, glyceryl trinitrate dilates the coronary arterioles and improves the blood supply to the heart in patients with angina pectoris, and atropine may relieve the pain due to a spastic colon. The pain of peptic ulcer may be quickly removed by antacids, and the pain of bacterial inflammation may be relieved by chemotherapy. Pain nerve pathways can be blocked, either temporarily by injection of local anæsthetics, or permanently by ethyl alcohol.

This article, however, is concerned with drugs that act primarily to ease pain, and they are conveniently divided into two well-known groups: (1) the antipyretic-analgesic group; (2) the morphine group.

The *antipyretic-analgesic group* comprises acetylsalicylic acid (aspirin), phenacetin, acetanilide, phenazone and amidopyrine. The new drug, butazolidin, probably also comes under this heading. The earlier members of this group were used primarily as antipyretics, and the salicylates were, of course, used in the treatment of rheumatic fever, as recently discussed by Professor Bruce Perry (1952) in this journal.

The antipyretic action is exerted on the temperature-regulating centre of the hypothalamus, the raised body temperature being reduced by cutaneous vasodilatation and sweating, both of which increase the amount of heat lost from the body. It has often been stated that aspirin relieves pain also by a central nervous action, but there is nothing to justify suggestions that it acts upon the thalamus, except that the latter is in some way concerned with the appreciation of pain and is closely related anatomically to the hypothalamus, in which the antipyretic action is located. The analgesic action of these drugs is clearly different from the undoubted central actions of morphine. Their effects are extremely useful in pain of 'rheumatic' character in joints, ligaments, or muscles, and in the relief of headache, but they are of no value in severe pain of traumatic origin or the pain of visceral colics, for which a morphine-like action is required. Aspirin also differs from morphine in that it does not raise the threshold to experimentally induced painful stimuli, and it is not a drug of addiction.

The mode, and even the site, of action of aspirin are quite obscure. From the fact that salicylates and cortisone act similarly in rheumatic fever it was suggested that the former act by stimulating the adrenal cortex to secrete a cortisone-like compound. There is little to support this view, but there is quite a possibility that the remarkable effectiveness of salicylates in this

disease is due to local actions on the rheumatic process, which in turn may be due to a reduction in capillary permeability (Swyer, 1948). Aspirin might also act locally in the relief of pain of other origins.

DRUGS CONVERTED TO N-ACETYL-*p*-AMINOPHENOL

It is important to remember that chemical substances may sometimes be converted into pharmacologically active agents as the result of metabolic changes in the body. For example, the original prontosil rubrum was shown to be changed in the body into the active sulphanilamide; castor oil, itself a positively soothing substance, becomes an irritant purgative when acted upon by lipase which splits off ricinoleic acid.

Brodie and Axelrod (1948) have shown that the antipyretic-analgesic actions of acetanilide and acetophenetidin (phenacetin) are probably due to the conversion of these substances to the substance, N-acetyl-*p*-aminophenol, which has been shown to have analgesic properties. This compound is also probably responsible for the formation of methæmoglobin, which occasionally follows the administration of acetanilide and phenacetin.

SALICYLAMIDE

It has long been known that salicylamide has central nervous depressant actions. Litter *et al.* (1951) have reported that oral doses of 2 g. were effective in relieving pain associated with rheumatoid arthritis, osteoarthritis and fibrositis, and that the drug was also active in rheumatic fever. It was claimed that it was better tolerated than salicylates and that it decreased the plasma prothrombin time. More accurate comparisons with other antipyretic-analgesics are obviously required. Mandel *et al.* (1952) have shown that salicylamide is excreted in the urine as a glucuronide. There is no evidence that it is converted to salicylate in the body.

PHENYLBUTAZONE (BUTAZOLIDIN)

Thus drug must be classed as a member of the antipyretic-analgesic group and appears to be the most potent of this type. Its actions were first studied in Switzerland, where it was produced by the firm of Geigy in a mixture called 'irgapyrin', which consists of 15 per cent. amidopyrine + 15 per cent. phenylbutazone in water. The preparation has been given intramuscularly, and occasionally intravenously, and Belart (1949), Gsell and Müller (1950) and others have reported good results from its use in the treatment of rheumatoid arthritis and other rheumatic states in which it was particularly effective in relieving pain. It was soon noticed that its effects were much longer lasting than those of amidopyrine.

It seems that amidopyrine is quite rapidly destroyed in the body, whereas phenylbutazone is eliminated very slowly.

The general pharmacological actions in animals of both 'irgapyrin' and of phenylbutazone were studied by Wilhelmi (1949), who found that the

latter was an effective antipyretic, reduced the inflammatory responses to ultra-violet irradiation by causing constriction of dilated capillaries, and was also an antihistaminic. It had no significant effects on circulation and respiration and appeared to be less toxic than amidopyrine.

The earlier accounts of the clinical effectiveness of 'irgapyrin' suggested to Currie that the phenylbutazone, which was being used mainly as a solvent for the amidopyrine, might be responsible for some of the relief obtained. Reports of the antirheumatic action of phenylbutazone given by itself appeared almost simultaneously in Britain (Currie, 1952) and in the United States (Kuzell *et al.*, 1952), and since then numerous accounts of the drug's action have appeared in the literature. All observers are agreed that phenylbutazone often relieves the pain associated with rheumatoid arthritis. It reduces joint tenderness, and in many cases increases the range of movement and reduces swelling. If there is fever the temperature will be lowered by the drug. Phenylbutazone has also been found to be effective in rheumatic fever, ankylosing spondylitis, osteoarthritis, gout and some of the less well-defined rheumatic conditions. There is no evidence that phenylbutazone acts like cortisone or ACTH since it does not significantly lower the erythrocyte sedimentation rate (Rhys Davies *et al.*, 1952), and there is no change in ketosteroid excretion, eosinophil counts or blood pressure. The objective signs of improvement in the joints are probably due to relief of pain and the consequent capacity for increased movements. Thus phenylbutazone is in essence a potent, long-lasting analgesic of the same general class as aspirin and amidopyrine.

The virtues of phenylbutazone must be balanced against its toxic actions, which probably occur in nearly 50 per cent. of patients. The toxic effects include nausea, vomiting, activation of peptic ulcers, melæna and hæmatemesis when the drug is given by mouth. Water retention may occur, producing œdema and even congestive heart failure. Blood disorders after its administration include aplastic anæmia, agranulocytosis and thrombocytopenia. Cutaneous eruptions of erythematous, maculo-papular, vesicular, purpuric or urticarial character have also occurred.

Phenylbutazone may be given either by intramuscular injection of a 20 per cent. solution, which is rather painful, or by mouth. One gramme daily is the usual initial dose, and with oral administration divided doses are best. After a few days, 1 g. may be given on alternate days for two to four weeks, and finally, 600 to 800 mg. on alternate days or even twice a week (Rhys Davies *et al.*, 1952). In order to reduce the likelihood of the development of sensitization reactions, such as skin eruptions and agranulocytosis, it is most important that the drug should be given in the smallest effective dose. It should only be used under careful medical supervision and patients should be warned of the possible toxic effects, particularly the symptoms, such as malaise, sore throat and fever, which might indicate the occurrence of agranulocytosis.

COMPARISONS OF SOME NEWER ANALGESIC DRUGS WITH MORPHINE

A number of new synthetic drugs has been investigated since the discovery of pethidine by Eisleb and Schaumann in 1938. Methadone (amidone, 'physeptone') was introduced in Germany during the war; phenadoxone ('heptalgin') is a closely related compound. These substances have recently been carefully compared with morphine for their effects in relieving chronic pain due to various causes (Nathan, 1952). This clinical trial has given some valuable information on the comparative potencies of these drugs. The usual 16 mg. ($\frac{1}{4}$ grain) dose of morphine sulphate has the same analgesic effect as 12 mg. of methadone hydrochloride or 125 mg. of pethidine hydrochloride, whether the drugs are given by mouth or by injection. When given by injection, 10 mg. of phenadoxone is equivalent to 16 mg. of morphine, but when given orally the former drug is so unreliable that no comparison with other drugs is possible: 1.5 ml. (25 minims) of the well-known morphine preparation, 'nepenthe', is equal to 16 mg. of morphine. Nathan suggests the following lower and upper limits of useful single doses of these drugs:—

Morphine.....11 to 65 mg. (1/6 to 1 grain), oral or parenteral
Pethidine .....50 to 250 mg., oral or parenteral
Methadone ..... 5 to 30 mg., oral or parenteral

The upper limits are, of course, determined by the occurrence of side-effects, which include drowsiness, lassitude, dulling of intellectual activity, dizziness, anorexia, nausea, vomiting and sweating. The frequency of side-effects is much greater in ambulant patients than in those confined to bed, this being particularly the case with regard to the nausea and vomiting produced by morphine. For example, Lee (1942) recorded nausea in only 3 per cent., and vomiting in 2.6 per cent. of bed patients in a cancer hospital, whereas Comroe and Dripps (1948) noted nausea in 40 per cent. and vomiting in 16 per cent. of ambulant subjects. Rubin and Winston (1950) have shown that morphine sensitizes the vomiting centre to vestibular stimulation, and that 100 mg. of 'dramamine' prevents this action of morphine.

The actions of these analgesic drugs on smooth muscle deserve mention. It is well known that morphine causes constipation by increasing the tone of the muscle and reducing the propulsive activity of the alimentary tract, and that pethidine and amidone are weaker in this respect (Vaughan Williams and Streeten, 1950). Indeed pethidine appears to reduce gastric and colonic tone, but it is nearly as potent as morphine in raising intrabiliary pressure and can sometimes induce attacks of biliary colic. This last action is presumably due to spasm of the sphincter of Oddi (Gaensler, McGowan and Henderson, 1948). Ureteric muscle is contracted by morphine (the spasm being prevented by simultaneous administration of atropine) and relaxed by pethidine.

MORPHINE DERIVATIVES

Diamorphine (heroin) is now regarded as the most potent of all drugs of

addiction and its manufacture and use have been forbidden in many countries. It has been omitted from the 1953 edition of the *British Pharmacopœia*. *Dihydromorphinone hydrochloride* ('dilaudid') is more potent but shorter-acting than morphine; *methyldihydromorphinone hydrochloride* ('metopon') is effective by mouth and has been much used in the United States, in doses of 6 to 9 mg., for the relief of pain in patients with terminal cancer. Both these morphinone compounds produce fewer alimentary symptoms than morphine, but both are drugs of addiction.

The structural formula of morphine is not yet known in its three-dimensional arrangement, but in 1946, Grewe synthesized a compound, *N-methylmorphinan*, which contains 4 of the 5 cyclic rings of the morphine molecule. A derivative, *3-hydroxy-N-methylmorphinan* (methorphinan, 'dromoran'), has recently been synthesized by Schnider and Grüssner (1949); its pharmacology has been studied by Randall and Lehmann (1950), and clinical reports on its actions have been published by Zager *et al* (1949) and others in the United States. Glazebrook (1952) has made the following points concerning its clinical actions and uses:—

(a) Of the two optical isomers, *L*-methomorphinan is the active agent. It is used as the tartrate.

(b) Methorphinan is effective in doses of 2 to 4 mg. It is as active by mouth as by injection. Its action lasts longer than that of morphine.

(c) Patients who were given both morphine and methorphinan usually preferred the latter. Methorphinan made patients feel cheerful the morning after an evening dose.

(d) Methorphinan has less hypnotic and sedative action than morphine, and is not suitable for allaying anxiety and restlessness. It is less active than codeine and methadone in depressing the cough reflex: 3 mg. of methorphinan depresses breathing as much as 16 mg. ($\frac{1}{4}$ grain) of morphine, and also induces as much spasm of smooth muscle.

(e) Methorphinan + barbiturates may produce severe respiratory depression.

(f) Methorphinan is to be regarded as a drug of addiction.

The final place of methorphinan as an analgesic will take time to establish, but it is clearly most useful to have alternative drugs for those patients who react unfavourably to any one drug of the group. It has now been amply shown that all the drugs of the morphine type which have powerful analgesic actions must be classed as drugs of addiction, and this has been recognized in this country by the restriction of their use under the Dangerous Drugs Acts. It is quite possible that a morphine-like analgesia can only be produced by drugs capable of causing addiction.

Depression of respiration is another feature of these potent drugs which so far appears to be inseparable from their pain-relieving properties. It is usually said that pethidine, in its ordinary therapeutic dosage, is less depressant to respiration than the others, and this is the reason given for its

widespread use as an obstetric analgesic. In adults, however, pethidine depresses breathing almost as much as morphine, so that its relative harmlessness to the new-born infant may be due either to its poor penetration through the placenta into the fœtal circulation, or to the fact that the neonatal respiratory mechanism is less sensitive than that of the adult to this drug.

N-ALLYLNORMORPHINE

An interesting development in this field is the demonstration of the antagonism of N-allylnormorphine ('lethidrone') to morphine. In this new compound the N-methyl group of morphine is replaced by an N-allyl group, and one might imagine that the antagonism is of the competitive type like that which underlies the antagonism of *p*-aminobenzoic acid to the antibacterial action of sulphonamides. The antagonism of N-allylnormorphine to morphine was first demonstrated by McCawley, Hart and Marsh (1941), who showed that the drug could overcome respiratory depression induced by morphine. Subsequent investigations by Unna (1943), Huggins *et al.* (1950), and Smith *et al.* (1951) in animals have shown that N-allylnormorphine also antagonizes other actions of morphine, e.g. analgesia in mice, general depression in dogs, and the characteristic excitation in cats. In addition, the drug antagonizes the respiratory depression produced by codeine, 'dilaudid', metopon and methadone, and in mice and rats it can protect against lethal doses of such compounds. The antagonism towards pethidine is less than that towards the other drugs mentioned.

The actions of N-allylnormorphine *in man* have been described by Wikler (1951), Eckenhoff *et al.* (1952a,b), and Fraser *et al.* (1952). In normal persons intravenous injection of 5 to 10 mg. depresses breathing and may lower the blood pressure and cause dysphoria. Wikler found that in ex-drug addicts subcutaneous injection of 30 to 75 mg. caused lethargy, drowsiness, vivid day dreams, and dysphoria which might amount to acute panic.

When N-allylnormorphine is given before morphine it prevents respiratory and circulatory depression, but the most striking effects have been observed when it has been given to overcome existing morphine depression. In such cases the stimulation of breathing occurs during the first minute after intravenous injection of N-allylnormorphine, reaches a peak within one to two minutes, and then declines gradually. If the blood pressure has been reduced by morphine the N-allyl compound will restore it to normal, but it will not raise a normal blood pressure. Eckenhoff *et al.* (1952a,b) state that the sedative effects of morphine are not antagonized. It is not yet clear how far the analgesic action of morphine in man is antagonized by N-allylnormorphine, although it is known that the analgesic action in animals may be abolished. When given to morphine addicts under the influence of this drug, N-allylnormorphine promptly induces withdrawal symptoms. The N-allyl compound has been successfully used in the treatment of patients with opiate poisoning, to whom it has been given intravenously in doses of 10 to

40 mg. It is important to realize that the effect of a single injection may not last for more than about one hour, and that subsequent injections of the drug become progressively less effective.

It has also been shown in man that N-allylnormorphine antagonizes the actions of 'dilaudid', metopon, methadone and pethidine.

Fraser *et al.* (1952) describe methadone poisoning in two patients who responded very quickly to the antagonist, respiration being markedly stimulated within a few minutes in both, and consciousness returning in five minutes in one of the patients.

It has been shown that N-allylnormorphine does *not* antagonize the central nervous depression induced by barbiturates, cyclopropane, diethyl ether or other factors, so it would appear that the actions of the drug are exerted only against those drugs which depress the central nervous system by a morphine-like action.

This action of N-allylnormorphine could be applied not only in the treatment of poisoning by the drugs mentioned, but also on occasions when it is desired to cut short a central depression within the therapeutic range. For example, in obstetrics, N-allylnormorphine might be given to the mother to antagonize analgesic drugs just before the child is born, or it might be injected into the umbilical vein of the new-born infant. These and other aspects need to be more fully investigated.

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REVISION CORNER

THE DIAGNOSIS OF EARLY PREGNANCY

THE clinical diagnosis of early pregnancy is often difficult. The cessation of menstruation in association with morning nausea and sickness, fullness and tingling in the breasts and frequency of micturition suggests an early gestation.

Such a diagnosis is presumed in the majority of cases if characteristic changes are also present in the breasts and reproductive tract. These changes are: enlargement of the breasts with the formation of Montgomery's tubercles; discoloration of the vaginal walls; softening of the cervix, and an alteration in the size, shape and consistence of the uterus. These symptoms and signs generally indicate an early gestation, but they do not furnish positive proof. Many attempts have been made throughout the years to devise a test which would accurately confirm an early gestation, but all proved unsuccessful. In 1926, however, the outstanding discovery of Aschheim and Zondek, and of Smith and Engle, that in the laboratory animal the anterior pituitary gland controls the activity of the gonads, not only stimulated an intensive study of reproductive physiology but also laid the foundation for a simple pregnancy test. Some two years later, Aschheim and Zondek found that the urine of pregnant women when injected into immature female mice produced an effect on the ovaries similar to that produced by anterior pituitary extracts. The infantile ovaries undergo marked development; they increase in size, and there is follicular and luteal growth associated with hæmorrhage into the follicles and in the stroma. This important finding formed the basis of the Aschheim-Zondek and subsequent biological tests for the detection of early pregnancy.

The substance or hormone present in pregnancy urine which promotes gonadal development was at first thought to be secreted by the anterior pituitary gland, but it is now known to be placental in origin and is termed chorionic gonadotrophin, or C.G. It is excreted in the urine during pregnancy and can be recovered from placental tissue. Chorionic gonadotrophin is secreted during the earliest days of pregnancy by the trophoblastoderm and later by the cytotrophoblasts of the chorionic villi.

The amount of hormone present in the urine increases rapidly following nidation of the ovum, reaching a peak of about 30,000 to 50,000 I.U. or higher between the 50th and 60th day after implantation. The urinary concentration then falls to a comparatively low level between the 12th and 16th weeks of pregnancy, which continues until about the 36th to 38th week, when a slight rise may occur.

The biological reactions produced by pregnancy urine are not specific; a similar reaction is obtained from the urine of women with chorionepithelioma and from the urine of men with embryonic testicular tumours. A positive reaction means that there is living chorionic tissue secreting chorionic gonadotrophin and generally indicates that a pregnancy does exist. The test becomes positive about ten days after conception, and remains positive in some cases up to seventy-two hours after delivery of the placenta (Crew, 1936). The test may continue to be positive after the fœtus dies *in utero*, or it may be positive when there is no fœtus present, as in hydatidiform mole. When the test is negative it may be assumed, apart from the exceptional case, that there is no active chorionic tissue in contact with the maternal tissues and that a pregnancy does not exist. A false

negative reaction is sometimes obtained between the 12th and 16th weeks of gestation, when the concentration of chorionic gonadotrophin falls to a low level.

BIOLOGICAL TESTS

The mouse was the test animal used in 1928 by Aschheim and Zondek, but since then considerable investigation has been carried out on other laboratory animals with a view to simplifying the procedure and obtaining a result in a shorter period of time (five days for the Aschheim-Zondek test) without interfering with accuracy. Several such tests have been evolved, the most important of which are the Friedman, the rat hyperæmia, and the Hogben tests.

Collection and detoxication of urine.—First morning specimens of urine give more accurate results, as they contain the hormone in highest concentration.

170 millilitres (6 ounces) of urine are usually requested and this should be dispatched to the laboratory in a clean container. Generally the urine is treated before injection, as many untreated specimens prove toxic to the test animal: 30 millilitres of urine are made acid to litmus paper with dilute HCl, and after the addition of 1 g. of sulphosalicylic acid the urine is filtered. Sodium bicarbonate is added to the filtrate, which is brought to a pH of 5.5 and is then ready for injection.

The Aschheim-Zondek test.—The test animal is the mouse.

Five 21-day-old female mice weighing about 8 to 10 g. receive a twice-daily subcutaneous injection of 0.4 ml. of urine for three consecutive days. The mice are killed on the fifth day, or 100 hours after the first injection, and the ovaries examined macroscopically.

Various reactions may be noted in the ovaries: (1) several large corpora lutea may have formed; (2) blood spots may be present on the ovaries; (3) large follicles may be observed—'white spots'. The uterus and vagina may also show varying degrees of enlargement. The presence in one or both ovaries, in one or more animals, of a corpus luteum or blood spot signifies a positive result. In very early pregnancy, and occasionally after the menopause, 'white spots' only, with some enlargement of the uterus, may be noted. These spots indicate an increase in urinary gonadotrophic hormone above normal, and in suspected early pregnancy the test should be repeated after an interval of ten days. The test gives an accurate diagnosis of pregnancy in 99.5 per cent. of cases. The Aschheim-Zondek has been the test mainly used, until within recent years, in the Pregnancy Diagnosis Station, Edinburgh.

The Friedman test.—The test animal is the rabbit. The isolated rabbit does not ovulate spontaneously, but ovulation can be induced within twenty-four hours by the intravenous injection of 'pregnancy urine' (Friedman, 1929).

The urine is detoxicated in a similar manner to that for the Aschheim-Zondek reaction, and 10 ml. of treated urine are injected into the marginal ear vein of two female virgin rabbits, or rabbits which have been segregated over a period of thirty days. At the end of twenty-four hours one of the rabbits is either killed or laparotomized, and the ovaries are inspected.

The presence of hæmorrhagic or ruptured follicles is adequate evidence of a positive reaction. If the result is negative the second rabbit is sacrificed after a further twenty-four hours and the ovaries examined. The Friedman test thus gives a result within twenty-four to forty-eight hours, with a reliability similar to that of the Aschheim-Zondek test.

The rat hyperæmia test.—Various investigators selected the immature female rat as the test animal. The subcutaneous injection of 'pregnancy urine' in the immature rat induces within a period of twenty-four to forty-eight hours

hyperæmia of the ovary and ovarian capsule, and the formation of hæmorrhagic corpora lutea. As ovarian hyperæmia was the earliest end-point noted, it was used as a criterion for a positive pregnancy reaction. A result was thus possible in six hours. Kupperman (1943) modified the test by injecting the urine intraperitoneally instead of subcutaneously and found that the accuracy—99.5 per cent.—was maintained when the ovaries were examined after two hours.

One or two immature 21- to 55-day-old female rats are injected intraperitoneally with 2 ml. of native urine, in divided doses of 1 ml. each into the right and left lower abdominal quadrants. The rats are killed at the end of two hours and the ovaries examined.

A reddish or pink appearance of the ovary and capsule signifies a positive reaction. This test is used routinely in many laboratories.

The Hogben test.—This test is based on the observation that the injection of anterior pituitary extracts promotes ovulation and oviposition in the female South African clawed toad (*Xenopus lævis*), which does not normally ovulate in captivity. A similar effect is induced by the injection of 'pregnancy urine'. The toad, however, is less sensitive to chorionic gonadotrophin than the mouse, rabbit and rat, and when it is used as the test animal it is advisable to delay carrying out the test until ten days after the first missed period.

As the *Xenopus lævis* is also sensitive to toxic urine it is advisable to inject an extract of the urine rather than treated or native urine. There are several methods of extracting the hormone, but the kaolin extraction procedure is both simple and satisfactory. A urine concentrate equivalent to 30 millilitres of urine is injected into the dorsal lymph sac of one or two female toads weighing 60 to 100 grammes.

Evidence of ovulation within a period of twenty-four hours indicates a positive reaction. The Hogben test, which gives an accuracy of 99.8 per cent., is now the routine procedure in the Pregnancy Diagnosis Laboratory, Edinburgh (Hobson, 1952).

The administration of 'pregnancy urine' has also a biological effect on the gonads of the male toad, in that it induces detachment and migration of spermatozoa; this reaction is used as a pregnancy test in some Continental and American clinics. Fluid from the external cloacal orifice is aspirated by a glass capillary pipette and examined microscopically for spermatozoa. If negative, an amount of filtered morning urine varying between 2 and 10 ml., depending upon the size and species of the toad, is injected into the dorsal lymph sac, and the fluid is aspirated from the cloacal orifice one hour later. The presence of spermatozoa in the fluid indicates a positive test.

CHEMICAL TESTS

Chemical tests have the advantage over those already described in that they do not involve the use of laboratory animals. They are not so accurate, however, as the biological tests, and on this account they are seldom used routinely.

The Kapeller-Adler test depends upon the identification of histidine, which is a normal constituent of the urine of women throughout pregnancy.

Bromine in acetic acid is added to a test tube containing 5 ml. of filtered acid urine until the original colour of the urine changes to orange-red, then orange-yellow, and finally, to pale yellow. After the addition of 0.5 ml. of a mixture of ammonia and ammonium carbonate, the test tube is placed in a beaker of boiling water for two or three minutes. Urines containing histidine turn red or reddish-violet; histidine-free urines do not change colour.

This test is said to be 100 per cent. accurate in normal pregnancy, but its value is compromised by the finding that 'non-pregnancy urine' sometimes gives a positive reaction.

The Guterman test is based on the colour reaction which develops when pregnanediol—an end-product of progesterone metabolism—is treated with sulphuric acid.

The pregnanediol present in 100 ml. of morning urine is extracted by a simple procedure. Concentrated sulphuric acid is then added to the pregnanediol; the development of an orange-yellow or deep yellow colour indicates a positive reaction. The result is available within three hours.

Guterman (1945) has found that the reaction is at least as accurate as that of the Friedman test, but this degree of accuracy has not been confirmed by other investigators.

CLINICAL TESTS

The clinical tests have the advantage over the biological and chemical tests in that they do not necessitate the use of either laboratory animals or chemicals. They do cause some inconvenience to the patients, however, and the results have not the same degree of accuracy.

Prostigmin.—The administration of prostigmin—a parasympathetic stimulant—in cases of delayed menstruation promotes hyperæmia of the uterine endometrium and is followed by uterine bleeding within seventy-two hours of the last injection (Soskin *et al.*, 1940). The pregnant uterus, however, does not react in the same way. It is such a vascular organ that prostigmin-induced hyperæmia causes little or no disturbance. In suspected cases of early pregnancy 1 mg. of prostigmin, or 1 ml. of 1:2000 prostigmin methyl sulphate, is given intramuscularly daily for three successive days. The absence of bleeding following the injections is indicative of a positive reaction. The test is accurate in 85 to 90 per cent. of cases. The administration of prostigmin may be associated with some side-reactions, such as giddiness, frequency of micturition and sickness. Severe collapse has been reported.

The Schwartz test.—In 1942, Zondek introduced a combined œstrogen-progestogen treatment for amenorrhœa of less than two years' duration. He found that the intramuscular injection of 2.5 mg. of œstradiol benzoate, combined with 12.5 mg. of progesterone, daily for two successive days, is followed, in a high proportion of cases, by vaginal bleeding within seven days of the last injection. The mechanism of the bleeding is probably similar to that induced by parasympathetic stimulants. Œstrogen and progesterone are given therapeutically, either singly or combined, in some complications of early pregnancy associated with bleeding, such as threatened abortion, with some measure of success. On this basis, Schwartz (1950) introduced the combined œstrogen-progestogen formula as a test for early pregnancy. The test is positive if no bleeding follows the intramuscular injection of 2.5 mg. of œstradiol benzoate, combined with 12.5 mg. of progesterone, daily for three successive days. Ampoules containing œstrogen and progesterone in the necessary proportions are available, such as 'disecron' (Schering). Schwartz found the test to be almost 100 per cent. accurate, but this high degree of accuracy has not been confirmed by other investigators.

Body temperature record.—It has been known for a long time that the body temperature varies during the menstrual cycle. Two distinct temperature records

are recognized—monophasic and biphasic—which are related to the type of menstrual cycle. In the absence of ovulation the temperature shows little variation throughout the cycle, but in ovulatory cycles the temperature rises a few fractions of a degree above the pre-ovulatory level, and this elevation is maintained until the onset of menstruation. The increase in body temperature during the second half of the menstrual cycle is a progesterone effect. When pregnancy supervenes, the temperature continues at the higher level until between the 16th and 20th weeks of pregnancy. This test is accurate and detects pregnancy at the earliest stage, but it is of limited value only, in so far as it involves daily temperature recording over a considerable period of time.

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NOTES AND QUERIES

Treatment of Plantar Warts

QUERY (from India).—I have several patients, all of them mill workers, who suffer from extensive bilateral plantar warts of several years' duration. The warts usually start over the head of the first metatarsal bone and in course of time spread over other areas of the foot. They are extremely painful and the pain is followed by severe burning sensations over the whole of the foot and oozing of small quantities of serosanguineous fluid. The cause of the condition is marked by remissions alternating with exacerbations. There is no history of venereal disease. Could you suggest an effective line of treatment which could be undertaken by a general practitioner?

REPLY.—There is no treatment which is 100 per cent. efficient in these cases of virus warts. That which most nearly approaches this figure is a simple but somewhat tedious method of using formalin. A 3 per cent. solution of formalin (itself 40 per cent. formaldehyde) in water is prepared. This is used to fill an eggcup or similar receptacle to the brim and the affected area of the sole is then applied to the cup so that the skin is soaked by the lotion. Plates, saucers, and the like are useless as the foot rests on the bottom and its pressure excludes the lotion from direct contact. This soaking must continue for a full ten minutes once a day. This is best timed by a clock as the period always seems unduly long. The foot is then dried without further washing. Once a week the superficial débris can be scraped away with a blunt knife. The used solution must not be poured back into the stock bottle, and the stock bottle must itself be refilled with fresh lotion once a week. The vast majority of cases are completely healed in a period which varies from three to eight weeks. The whole foot should never be immersed as the thinner skin on the sides and top of the foot easily acquires a formalin dermatitis.

SYDNEY THOMSON, M.D., F.R.C.P.

Postural Cough in Chronic Bronchitis and Emphysema

QUERY.—A patient, aged 59 years, suffering from chronic bronchitis and asthma, is troubled while he is up by a frequent bubbling, distressing cough, productive of a moderate amount of clear frothy mucus. As soon as the patient lies down the cough ceases. An x-ray shows some fibrosis of the lungs and emphysema at the bases. The effect of posture on the cough is definite and clear-cut, and I should be grateful if you could suggest an explanation and possible

treatment. A course of penicillin and streptomycin inhalations six months ago cleared up the bronchial symptoms, but these have now returned.

REPLY.—Two pathological conditions of the respiratory tract give rise to symptoms which are commonly associated with posture. One is paranasal sinus infection, and the other is bronchiectasis. Symptoms from the former tend to be aggravated rather than relieved by lying down. Bronchiectasis involving one or both upper lobes might be the cause of a productive cough when the patient is upright, as sputum from these lobes would gravitate into the main bronchi with resulting stimulation of the cough reflex. Variable degrees of bronchial or bronchiolar dilatation are common in patients with chronic bronchitis, and if the x-ray shows fibrosis to be present such dilatation is very likely. Such a theory would explain why the patient had benefited temporarily from inhalations of penicillin and streptomycin.

Full investigation of the upper respiratory tract including x-ray of sinuses, is advisable. Likewise investigation of the bronchial tree with opaque medium (bronchography), particularly of the upper lobes, should be considered, provided that the degree of emphysema is not severe. Bronchography may be dangerous in the presence of gross emphysema. Any bronchiectasis so defined should be treated by twice daily postural drainage, aided by percussion over the affected area, and breathing exercises under expert supervision. Further antibiotic therapy, either by inhalation or injection, would also be justified, particularly as it had previously relieved symptoms for a considerable time.

E. M. BUZZARD, B.M., F.R.C.P.

Ergotamine and Migraine

QUERY.—Could you inform me whether treatment with ergotamine tartrate or dihydroergotamine is only palliative, or curative, in migraine? If curative, what is the percentage of cures? When such treatment fails, what are the causes of failure? After how many doses (or total quantity given) may it be assumed that the drug has failed?

REPLY.—Ergotamine tartrate and dihydroergotamine have been found to be roughly equally effective in the treatment of the acute attack, there being complete relief in 70 to 80 per cent. of cases of typical migraine when the drug is given subcutaneously or intramuscularly. When given by mouth the results are about half as good and nausea and vomiting are more prominent. Attacks tend to become less frequent with advancing years but there is no reliable evidence that this process is accelerated by treatment with ergot alkaloids. Toxic reactions may prevent further use. In a recent series these occurred in 18 out of 40 cases with subcutaneous injection of ergotamine tartrate and led to discontinuance of treatment in five. The corresponding figures for 40 cases treated with dihydroergotamine were six and one. The chances of relief are increased by early administration and the injection may be repeated, if necessary, at hourly intervals for one or two hours. The initial dose of dihydroergotamine methanesulphonate should be 0.5 mg. but may be increased to 1 or even 2 mg. in subsequent attacks, if well tolerated.

R. S. STACEY, M.D.

Headache due to Thyrotoxicosis

QUERY.—My wife has suffered from severe headaches since the birth of her second child, nine weeks ago. They are mainly behind the eyes and their onset and cessation are often extremely rapid. There is no nausea or vomiting and they are unrelieved by the simpler analgesics. In particular the headaches come on about 8 a.m. and often last into the afternoon. She is feeding the baby herself, and suffered from similar headaches after her first confinement, which disappeared when the baby was weaned. During this second pregnancy, she showed signs of thyrotoxicosis, and although these have diminished, there is still some proptosis, and thyroid enlargement. The headaches are accompanied by conjunctival injection. Could these be due to changes in, and around, the pituitary, and if so, can you recommend any treatment?

REPLY.—In answering this question I assume that all the ordinary causes of headache have been excluded. If this is so, it seems probable that the headache is the result of thyrotoxicosis. This is made more probable by the fact that proptosis is present and that the headaches are accompanied by conjunctival injection. It is difficult to make any recommendations for treatment without a far more exact knowledge of the patient's condition. If the thyrotoxicosis is extremely mild it might be possible to keep it under control by means of one of the antithyroid drugs. The relationship of the pituitary to thyrotoxicosis in general and to the eye signs in particular is still the subject of controversy.

RAYMOND GREENE, D.M., M.R.C.P.

Granular Lids

QUERY (from India).—What is a reasonable treatment, both in regard to time and cost, for

'granular lids' in school children? A colleague gave me a schedule of treatment the other day which is said to be very effective. It involves the local application of aureomycin ointment two-hourly for three weeks, and sulphamezathine by mouth in large quantities. I can only think that his hospital is far richer than mine, and his school authorities more complacent. Information at our jungle level on this point would be most valuable.

REPLY.—It is presumed that by 'granular lids' in school children is meant chronic trachoma, which I know by experience is common in India. Granular lids are by no means always due to trachoma and are often diagnosed as such on account of symptoms of ocular irritation, so common in tropical countries from exposure of the eyes to heat, glare, dust and wind. The diagnosis of trachoma may be difficult. On eversion of the upper eyelid trachoma is suspected with the finding of papillæ or follicles and blebs on the superior tarsus and upper fold of the fornix; it is confirmed by the presence of pannus (superficial vascularization) on the upper part of the periphery of the cornea. Ptosis of some degree is usually present. It should be realized that trachoma may progress for months or years, and treatment should be directed towards promoting the disappearance of the follicles without causing the formation of an excessive amount of scar tissue. This is best accomplished by the local application of 1 per cent. aureomycin or chloramphenicol, or terramycin drops or ointment if available, for two to six weeks. As these are not available I suggest the following line of treatment:—

The first essential is that the children should be placed under as favourable sanitary and hygienic conditions as possible. If there is much discharge from the eyes, which denotes a secondary infection, this should first be eliminated by the oral administration of a sulphonamide: sulphamezathine, in an initial dose of 0.5 g. for a child, with a maintenance dose of 0.25 g. three times a day for seven days.

The instillation of a few drops of weak zinc sulphate solution (1 grain to the ounce (65 mg. to 28.5 ml.) of distilled water) twice a day into the eyes of all infected children for three to six months, and the painting of the inverted eyelids with 30 per cent. sodium sulphacetamide solution once a day for two weeks every three months. The local application of 6 per cent. sodium sulphacetamide ointment at bedtime is also recommended. The drops can be instilled by the teacher, but the painting should be done by the medical practitioner. If a corneal ulcer develops in the course of treatment, the zinc drops are temporarily replaced by 1 per cent. boric lotion or normal saline lotion, and the sodium sulphacetamide paintings and ointment continued. Children with exuberant follicle or papillary formation on the upper tarsal conjunctivæ should be sent to the nearest hospital for evacuation of the follicle contents under local anæsthesia by some mechanical means such as rubbing them with a mounted swab, which is moistened with the sodium sulphacetamide solution, or by squeezing the tarsus between the blades of an expression forceps or the sharp spoon.

Excision of the upper transitional fold of conjunctiva is often advisable. This removes the disease-bearing part of the membrane, is a simple operation and produces a speedy cure. A preliminary ballooning of the fornix by a subconjunctival injection of an anæsthetic fluid (1 per cent. novocain in distilled water) renders all the above measures easy and painless.

Unfortunately there is no drug which is a specific for trachoma, and the treatment is prolonged and often painful. Fortunately many cases are mild and so the lesions are slight. Care should be taken to avoid the excessive use of irritant solutions such as copper and silver. The application of the copper stick to the tarsal conjunctiva has no place in the modern treatment of trachoma and should be discarded.

E. W. O'G. KIRWAN, C.I.E., M.D., M.SC., F.R.C.S.I.

Treatment of Furunculosis

DR. ENID M. GLEN (South Africa) writes.—In the February number of *The Practitioner* there is a query concerning treatment of furunculosis in the back of a patient's neck (p. 199). During the war when working in the Dermatological Department of the London Hospital, an increase in these cases occurred. It was thought to be due to the hair oil, manufacturers substituting mineral oils for vegetable oils in their formulæ. There was one brand of hair oil which seemed to be the chief culprit. In my own practice, I always inquire what hair oil is being used and, if necessary, substitute pure arachis oil, or a tragacanth preparation. The condition at once begins to clear up, and can be helped by often repeated applications of U.V.R. In my opinion, it is really an oil acne, similar to that met with in engineers and is due to the cutting mineral oils. The vegetable oils do not seem to cause it.

I suggest that in your patient's case the furunculosis of the nose is due to the fingers, which have been in contact with the neck (which often itches slightly), being used to 'pick' the nose.

PRACTICAL NOTES

Isoniazid in Lupus Vulgaris

THE results obtained with isoniazid, given for at least four months, in 15 patients with lupus vulgaris are reported by G. B. Dowling and his colleagues (*Proceedings of the Royal Society of Medicine*, March 1953, **46**, 163). Fourteen of the patients had had prolonged treatment with calciferol and had either relapsed or had proved resistant to treatment. The daily dosage of isoniazid was 3 mg. per kg. body weight for two months, and then 6 mg. per kg. body weight. All the patients, with the exception of one in whom treatment had to be suspended because of toxic effects, showed 'striking improvement' within one month. After four months' treatment, only two showed any clinical evidence of activity. Toxic effects occurred in four patients: (i) vertigo and a coarse tremor of the hands within a week; (ii) extreme fatigue and numbness of the head after two months; (iii) fatigue and an enormous appetite, with a gain in weight of 14 lb. (6.5 kg.); (iv) erythema nodosum and congestion of the lupus area. It is stated that 'the speed and reliability of this treatment have greatly exceeded that of calciferol and of calciferol with streptomycin', but the authors are now switching over to a combination of isoniazid and streptomycin. Brian Russell and N. A. Thorne (*Ibid.*, p. 165) have treated 15 patients for periods varying between nine and thirty weeks, their usual dosage being 100 mg. thrice daily. They have also given the drug by 'local intralesional injections' and by a combination of the oral and intralesional routes. Only one of their patients failed to show improvement, and in 12 it was either marked or moderate. They state that 'with oral treatment, a steady and quiet improvement takes place, without early exacerbations such as are often observed with calciferol'. J. Sommerville and J. A. Milne (*Ibid.*, p. 168) have treated 26 cases for periods ranging from seven to thirty-two weeks, with a daily dosage of 250 mg. None failed to respond to treatment: seven were clinically cured, eight almost so, 'the remainder showing varying degrees of progress'. In all of the fourteen cases examined histologically, there was 'evidence of regression of the lesion'.

Heparin in Arteriosclerosis

THE effect of heparin in the treatment of advanced peripheral atherosclerosis has been studied in 13 patients by H. Engelberg and J. B. Massell (*American Journal of the Medical Sciences*, January 1953, **225**, 14). In none of the patients was there a palpable arterial pulse at the popliteal or ankle level, and in all the oscillometric index below the knee was markedly reduced. Eleven had intermittent claudication, five had diabetes mellitus and eight had coronary atherosclerosis. Heparin was given intravenously in doses of 100 mg. intravenously two or three times weekly over a period of six months. During the first few months the Lee-White coagulation time was determined after each dose of heparin but, as the clotting time always returned to normal from four to seven hours of each injection of heparin, the authors consider that 'when heparin is given intermittently in this manner it is not necessary to follow the coagulation times'. No serious toxic reactions or hæmorrhages occurred in any of the patients. Results were assessed by digital plethysmography and by walking tolerance tests. In three extremities the digital flow was unchanged; in three it was decreased, but in two of these there was a marked improvement in walking tolerance; in eight extremities the digital flow was increased—in six the increase was more than 100 per cent. In eight of the ten patients in whom the walking tolerance test could be performed, there was improvement ranging from 17 to 800 per cent. Generally, the improvement in the peripheral circulation occurred gradually and progressively over the period of observation. It is suggested that the beneficial action of heparin in these cases is due to its effect in altering the lipoprotein spectrum of the blood and thereby retarding the development of atherosclerosis in the arteries. 'On the basis of these preliminary observations' the authors 'feel that the intermittent administration of heparin is a promising form of therapy for peripheral atherosclerosis'.

DOCA and Postspinal Headache

SUCCESSFUL results are claimed by R. I. Pfeffer (*American Journal of Obstetrics and Gynecology*, January 1953, **65**, 21) from the use of deoxycortone acetate (DOCA) in the treatment of postspinal headache. Of 300 patients who received saddle back anæsthesia, 70 developed postspinal headache. Thirty-five of these patients were treated by 'conventional methods', e.g., caffeine with sodium benzoate and other stimulants, ergot derivatives, codeine. 'This treatment was, in the main, unsuccessful'. The remainder were given sublingual tablets of DOCA, each containing 2 mg. of DOCA in 'a polyethylene glycol base'. The dosage was one tablet every four or six hours as necessary. Thirty of these patients (86 per cent.) obtained complete relief, and three were partially relieved. The two who were not relieved by DOCA were relieved by codeine. Relief was

usually obtained within thirty to sixty minutes, and as a rule treatment had to be continued for only one or two days. No side-effects were noted. It is suggested that the action of DOCA may be 'to elevate spinal fluid pressure by raising the concentration of serum sodium and thereby increasing extracellular fluid. Other possibilities are the "pressor" principle of DOCA or a proposed reciprocal effect via the anterior pituitary causing increased production of fluid by the choroid plexus'.

Massive Doses of Vitamin B_{12}

THE effect of massive single injections of vitamin B_{12} in the treatment of pernicious anæmia has been investigated by E. H. Reisner, Jun., and L. Weiner (*Blood*, January 1953, **8**, 81). Fourteen patients with pernicious anæmia in relapse were given a single intramuscular injection of 1000 μg. of crystalline vitamin B_{12}. Complete hæmatological remission resulted in 13. The patients were then followed without further treatment until hæmatological relapse occurred. Four patients had not relapsed at the time of their last visit four, six, eight and nine months after treatment; the remainder had all relapsed within periods of three to seven months. Seven patients with 'combined system disease that had shown no change after months to years of conventional therapy' which had maintained a normal blood picture, were given weekly injections of 1000 μg. of vitamin B_{12} for periods of four to thirteen weeks. In none of these was there any convincing evidence of improvement as a result of the administration of B_{12}. The authors conclude that 'massive single injections of vitamin B_{12} cannot be substituted for more frequent regular injections of smaller doses in the treatment of pernicious anæmia, without the danger of relapse and the aggravation of central nervous system disease. Furthermore, there is no evidence to indicate that a greater degree of improvement follows the regular weekly injections of massive doses of vitamin B_{12} to patients with chronic combined system disease than occurs with regular conventional doses. This is probably because amounts of B_{12} above a threshold value of 25 to 50 μg. by injection are rapidly and quantitatively excreted in the urine'.

The Effect of Cortisone on the Rheumatic Heart

THE effect of cortisone on the rheumatic heart has been studied by A. Golden and J. W. Hurst (*Circulation*, February 1953, **7**, 218) in a 10-year-old girl who died of congestive heart failure six months after her first attack of rheumatic fever. She was given 100 mg. of cortisone eight-hourly during the eight days immediately preceding death. There was no clinical response to this therapy. She had also had ACTH and cortisone at the beginning of the illness. At necropsy the striking finding in the myocardium was that 'the acute lesions consisted of extensive areas of interstitial fibrinoid degeneration of collagen, but there was remarkably little or no cellular reaction. Large mononuclear Aschoff cells were completely absent . . . None of the older healing lesions differed significantly from those seen in rheumatic carditis not treated with adrenocorticotropic hormone or cortisone'. It is suggested that these atypical acute lesions represent 'a suppression of cellular reaction to altered collagen'. Although the authors consider that their 'findings do not indicate that the injury to connective tissue associated with rheumatic fever has been prevented to any degree', they suggest that possibly 'prolonged suppression of inflammatory reaction might result in decreased scar tissue formation when final healing has occurred'.

Effect of Infective Diseases on the Tuberculin Reaction

THE effect of certain infective diseases upon the tuberculin reaction has been investigated by J. W. Bentzon (*Tubercle*, February 1953, **34**, 34). All patients admitted to Blegdams Hospital, the contagious diseases hospital for Copenhagen, between January and April 1951 had a Mantoux test done on, or soon after, admission, and again, whenever possible, two or three months after discharge. Depression of the reaction was found to be produced by measles, scarlet fever and infectious mononucleosis, whereas upper respiratory infections, acute tonsillitis, pneumonia, gastro-enteritis and paradysentery had little, if any, effect on the reaction. The depressive effect was most marked in the case of measles: of 31 patients whose reactions to the follow-up test were positive, 17 had no palpable induration to the first test, 8 had indurations measuring 1 to 4 mm., and in 6 the reactions were positive (i.e., induration of 5 mm. or more). In scarlet fever the depressive effect was less marked: of 48 patients with a positive follow-up reaction, 10 had no induration, 17 had indurations of 1 to 4 mm., and 21 were positive when tested on admission. Of the 25 patients with mononucleosis who had positive follow-up reactions, 14 were positive when tested during the early stage of the disease. The author concludes that 'the results of this study suggest that a negative reaction during the acute stage of measles, scarlet fever or infectious mononucleosis should be regarded as unreliable. It follows that in patients suffering from any of these diseases a diagnosis of tuberculosis should not be excluded nor a

BCG-vaccination performed on the basis of a negative tuberculin reaction'.

False Positive Urinary Tests Produced by Antibiotics

ATTENTION is drawn by R. W. Lippman (*American Journal of Clinical Pathology*, December 1952, **22,** 1186) to the fact that false positive tests for proteinuria and glycosuria can be obtained during the administration of certain antibiotics. He investigated the effect of streptomycin, aureomycin, chloramphenicol, terramycin and penicillin on the Benedict test for sugar and the salicylsulphonic acid test for proteinuria. At a concentration of 10 mg. per millilitre, streptomycin, aureomycin, chloramphenicol and terramycin gave a weak or moderately positive reaction with Benedict's solution, but none gave a positive reaction with 20 per cent. salicylsulphonic acid. Crystalline potassium penicillin G at concentrations of 100,000 and 25,000 units per millilitre gave strongly positive reactions with salicylsulphonic acid, but no reaction with Benedict's solution. It is pointed out that 'the concentrations of the antibiotic agents that gave positive tests for protein and reducing sugar might be attained in the urine after large therapeutic doses of these agents have been administered. This possibility must be considered in evaluating the urinary findings of patients who have been so treated'.

Hyaluronidase in Intramuscular Pyelography

THE following technique for intramuscular pyelography has been found by L. Dixon (*Radiography*, January 1953, **19,** 7) to be 'a most useful alternative' in cases in which, for some reason or other, the intravenous route is impracticable. 'This was particularly so in the case of children and babies and widens the scope of pyelography considerably'. The patient is prepared exactly as for intravenous pyelography. Diodone, 35 per cent., is the contrast medium used and, for each 20 ml., 1000 Benger units of 'hyalase' (a preparation of hyaluronidase) are added in the syringe. The total quantity injected intramuscularly is 10 to 20 ml. for children (according to age) and 20 to 40 ml. for adults (according to body weight). This is given undiluted and divided between the right and left buttocks. 'The pain which always occurs with intramuscular injections' passes off after about five minutes; 'if preferred, however, 1 ml. of 1 per cent. procaine may be added, which should make the injection almost painless'. Absorption of the diodone is very rapid. Films are taken 10, 20 and 30 minutes after the injection. Of the 12 cases (11 children and 1 adult) examined by this method it is said that 'no complications of any kind have occurred. In all cases visualization and structural detail have been adequate and comparable in every way with those obtained by the intravenous route'.

An Antidote to Smoking

'SMOKING appeal was effectively reduced', according to W. L. Gould (*GP*, February 1953, **7,** 53), in 77 per cent. of 349 smokers following the use of a medicated lozenge. The lozenge contained benzocaine, 1/20 grain (3 mg.), and was flavoured with saccharin, extract of liquorice, powdered ginger, and oils of anise, wintergreen, peppermint, coriander, and cloves. The recommended method of use is to take a lozenge every time there is a desire to smoke. The average number of lozenges taken by the subjects of this investigation was six daily, but some took as many as fifteen. There were no untoward effects. The safety of the lozenges is emphasized, and it is pointed out that even if 63 lozenges were taken at one time, this would represent 3 grains (0.2 g.) of benzocaine, whereas the pharmacological dose is 5 to 10 grains (0.3 to 0.6 g.). The anti-smoking action of the lozenge is attributed to: (a) its effect upon taste, and the effect of the small amount of benzocaine in the lozenge is to delay the absorption of the flavouring agents and thereby prolong their effect; (b) it satisfies the smoker's desire to have something in his/her mouth.

Deodorant Properties of Chlorophyll

TO investigate the deodorant properties of chlorophyll, D. M. Bryce and R. M. Savage (*Pharmaceutical Journal*, March 21, 1953, **170,** 209) used a solution of 15 mg. of not less than 95 per cent. sodium chlorophyll in water, which was sprayed on to two cotton-wool pads, each weighing 17 g. One of these pads was soaked with 20 ml. of decomposing bovine blood, and the other with 40 ml. of the same blood. Two pads to which no chlorophyll had been added were treated in the same way, to act as controls. The pads were then placed in boxes in which was a small hole, and 139 people were asked which box of each pair smelled less. The results were as follows:—

Odour	20 ml. solution	40 ml. solution	Total
Less with chlorophyll	51	59	110
No difference	8	2	10
Worse with chlorophyll	10	9	19

Distributing the 10 undecided results equally between the classes and applying standard tests of significance, the authors conclude that 'this result would have happened by chance less than once in 2000 million such trials, and is therefore highly significant'.

REVIEWS OF BOOKS

Influenza (and other Virus Infections of the Respiratory Tract). By C. H. Stuart-Harris, M.D., F.R.C.P. London: Edward Arnold & Co., 1953. Pp. iv and 235. Figures 98. Price 30*s*.

Dr. C. H. Andrewes, whose name will be closely linked with that of Professor Stuart-Harris whenever influenza is mentioned, in his foreword to this admirable and comprehensive book, draws attention to the fact that it has been written by a clinician whose laboratory and research knowledge of virus infections, particularly influenza, is unrivalled in this country and indeed in the world. Such a strong combination of knowledge cannot fail to produce a good book. Not only is it a good book, but it is a useful and practical book. True influenza infection is withdrawn from the rubbish heap on to which it is so often dumped, disguised and covered up by much clinical rubbish, and the features of influenza, both complicated and uncomplicated, are clearly described. Emphasis is laid upon the secondary bacterial complications, which are all important and on the necessity for culturing the organisms concerned. These organisms may be of several kinds and each one may be sensitive to a different antibiotic agent, so that blind treatment with antibiotics is often wasteful and useless, whereas the right antibiotic may be life-saving, particularly in the elderly. Attention is drawn to the occasional fulminating case, often in a young adult, seen in most epidemics, and it is disturbing to have confirmation of the fact that even the latest antibiotics often fail to influence the infection. The author has treated a few cases with staphylococcal antitoxin and with influenza convalescent serum, as well as with the latest antibiotics. Chapters are devoted to other specific virus infections such as psittacosis and Q fever, which are of more than diagnostic interest to the clinician now that aureomycin and terramycin are widely available. Perhaps the most ambitious chapters are those devoted to the less severe but more widespread virus infections, with the common cold as the villain of the piece. A praiseworthy effort is made to classify these catarrhal infections and to separate them from clinically allied bacterial infections of the upper and lower respiratory tract.

This book is very readable and contains a wealth of facts which are not only of interest to laboratory and research workers, but are of vital clinical importance to clinicians, especially to general practitioners who meet with the majority of the infections described in their everyday work.

Clinical Neurology. Edited by Frank A. Elliott, M.B., F.R.C.P., Brodie Hughes, Ch.M., F.R.C.S. and J. W. Aldren Turner, D.M., F.R.C.P. London: Cassell and Company, 1952. Pp. xxii and 751. Plates 8. Price 42*s*.

There has long been a need for a textbook of neurology of reasonable size and representative of the British outlook on the subject. This volume embraces a very wide field of neurology. Section 1 (nine chapters) is devoted to a somewhat sketchy outline of the physiology and anatomy of the nervous system, in the course of which a certain number of inaccuracies appear; a chapter on epilepsy which is too brief; a discussion of syndromes and a method of examination. Of fourteen pages devoted to clinical examination seven are allowed for the fields of vision alone. The whole of this section is too reminiscent of a synopsis. In section 2 the various clinical disorders of the nervous system are described; the sections on vascular malformations, infections, tumours and head injuries are well-balanced, precise and accurate. Throughout the volume there is a rather pronounced tendency toward syntactical error and the misuse of words, among the latter 'pathology' and 'case' are frequent offenders. This tendency is sufficiently marked to disturb the reader who appreciates prose style in his medical reading. The book is a useful one, but its use would be greatly enhanced by the omission or complete reconstruction of the first section.

Modern Trends in Forensic Medicine. Edited by Keith Simpson, M.D. London: Butterworth & Co. (Publishers) Ltd., 1953. Pp. x and 327. Figures 133 and 2 plates. Price 60*s*.

This is the work of eleven contributors designed to review—for the pathologist who is entrusted with medico-legal autopsies, for the forensic science worker and for the barrister—the last ten years' experience in the subject. Its object is to illuminate forensic problems and modern trends in the evaluation of such evidence. Attention has been restricted to fields in which change or re-assessment has been notable, or in which a ponderous or equivocal literature has accumulated. The field covered includes such subjects as the forensic aspects of stillbirth and neonatal death, pathology of the lung in those subjects, investigation of sudden death, changes following death, exposure to cold, starvation and neglect, together with problems in reconstruction of human skeletal remains, in-

cluding the dental aspects. On the laboratory side, the forensic aspects of blood groups, physical aids in criminal science, and recent advances in toxicological analysis receive consideration. The book contains a considerable amount of valuable and interesting reference material. A few statements are rather difficult to accept; for example, 'It remains that the twenty-eighth week of gestation is not difficult to assess with fair accuracy—largely from the simplest measurement of all, the crown-heel measurement of length'; 'Maturity has a medical bearing on the matter: the larger child might be expected to exhibit the more vigorous and sustained efforts to live and to resist harm', and, in treating the subject of precipitate labour, 'Careful examination of the skin of such an infant will often show the marks of gripping hands on the victim in order to effect a grip for a swing to inflict head injury'. The section on recent work on changes after death embodies some unusual findings and one wonders whether these have been influenced by the war conditions experienced in life by the subjects whose bodies were examined after exhumation. Factors associated with the burial also require close consideration in the interpretation of some of these findings. The long chapter on reconstruction of the human body is very well treated and incorporates extensive and important reference data.

The work is well and copiously illustrated and the photographs and plates have reproduced effectively on a paper of excellent quality. This is a valuable reference book which can be recommended and should find a place in the library collections of all who practise this subject.

Pediatrics in General Practice. By James G. Hughes, M.D. New York: McGraw-Hill Book Company Inc., 1952; London: McGraw-Hill Publishing Company Ltd., 1953. Pp. xiii and 735. Figures 178. Price $14.0 (119*s.*).

In the United States the general practitioner pædiatrician exists in large numbers, taking care of the younger members of the family. This volume is essentially a textbook for them, for it goes much further into detail than would generally be considered necessary in Great Britain. For example, there is a chapter on the problems of fluid and electrolytic balance which goes far beyond what even many hospital consultants in this country would consider essential knowledge for everyday use. Thus the book is really a work of reference and the title is a misnomer. Random sampling suggests that it is a thoughtful book, full of the results of practical experiences, written clearly, and the index makes reference easy. Printed in double columns and running to over seven hundred pages the book contains a large amount of information. As is so common in American books today, the bibliographies are almost exclusively confined to American publications and this form of isolationism is unfortunate. The foods recommended and the names of some of the drugs will also be strange outside North America. Nevertheless, English readers will find it a useful account of pædiatrics as taught today in the United States.

The Practical Management of Pain in Labour. By W. D. Wylie, M.B., M.R.C.P. D.A. London: Lloyd-Luke (Medica Books) Ltd., 1953. Pp. xii and 148. Figures 42. Price 18*s.* 6*d.*

The title is not misleading; it is a practical book. It is written by an experienced and senior anæsthetist to help those who have the responsibility of easing the pain of labouring women either in their own homes with minimal equipment, or in Maternity Centres with a choice of all modern analgesic and anæsthetic aids. No aspect of the subject is neglected, even to the relief of pain in thrombophlebitis by local infiltration of sympathetic ganglia, and the treatment of anuria by spinal, extradural and splanchnic techniques. Drugs and methods are concisely assessed and tables of comparison make it easy for the reader to see at a glance the relevant advantage and disadvantage. Due emphasis is given to those dangers which could so easily lead to maternal and fœtal death and, where they exist, alternative safer procedures are described.

It is remarkable how much sound sense and instruction has been condensed into a very readable book of less than 150 pages. It ought to be read with profit by every obstetrician and midwife as well as by anæsthetists, experienced or otherwise, who believe with the author that:

> 'Better by far you should forget and smile
> Than that you should remember and be sad'.

Trichlorethylene Anæsthesia. By Gordon Ostlere, M.B., B.Chir., D.A. Edinburgh: E. and S. Livingstone Ltd., 1953. Pp. viii and 83. Figures 5. Price 7*s.* 6*d.*

Trichlorethylene was first described in 1864 and its clinical use in anæsthesia and analgesia in this country was first introduced by Langton Hewer in 1939. Since then, the drug has been regularly used and by 1948 over a million administrations had been given in Great Britain. A small number of fatal cases have been associated with its use but in the opinion of many anæsthetists the dangers have been overemphasized. The publication of this book will

do much to restore confidence in its administration, as the causes and treatment of any hazards associated with its use are fully explained. This book is well arranged and produced, and the illustrations are adequate and clearly printed. There is an excellent chapter on the use of trichlorethylene analgesia in obstetrics which we recommend to general medical practitioners who are interested in midwifery.

Ophthalmic Pathology: An Atlas and Textbook. EDITED BY JONAS S. FRIEDENWALD, *et al.* Published under the joint sponsorship of The American Academy of Ophthalmology and Otolaryngology and the Armed Forces Institute of Pathology. Philadelphia and London: W. B. Saunders Company, 1952. Pp. ix and 489. Plates 240. Price 90*s.*

TEXTBOOKS on ophthalmic pathology seldom appear and only one such work has been published in this country in the last forty years. This new and comprehensive book compiled by eight distinguished Americans will be generally welcomed and should fill an obvious gap in the library of British-speaking ophthalmologists. The first three chapters deal briefly with the anatomy and physiological changes in the eye from the angle of the pathologist, and the remaining 400 pages cover inflammatory, degenerative, developmental, and neoplastic abnormalities in considerable detail. In a book of this type success and practical value depend largely upon the illustrations, which in this case are throughout of excellent quality and adequate number. The general production is of the highest standard and an efficient index is provided so that the book may readily be used for reference purposes. The text is so easily readable, however, that candidates for the final F.R.C.S. in ophthalmology will find it a valuable textbook. The authors and the sponsors are to be congratulated on the production of this work which can be thoroughly recommended to senior students, and indeed to all practising ophthalmologists.

Contact Lenses: Clinical and other Observations. BY J. M. ANDERSON, M.D. Brighton: Courtenay Press Ltd., 1953. Pp. 40. Figures 5. Price 7*s.* 6*d.*

THIS short work appears rather to fall between two stools, although on either side there are compensations. On the one hand, those who are sufficiently familiar with the theory and practice of contact lens work to follow the writer's arguments will learn nothing new, although they will find the historical outline interesting, and the list of references of value. On the other hand, those who have little or no knowledge of contact lens techniques will find the exposition somewhat esoteric, but they will be encouraged by the case reports detailed in the work. The monograph is illumined by the obvious enthusiasm of the author, and in these days of centralization it is a useful advertisement of the value of small specialized departments in regional hospitals.

Nutrition and Health. BY SIR ROBERT MCCARRISON, C.I.E., M.D., D.SC., F.R.C.P., with a postscript by H. M. SINCLAIR, D.M. London: Faber and Faber Ltd., 1953. Pp. 125. Figures 8. Price 12*s.* 6*d.*

SIR ROBERT MCCARRISON'S Cantor lectures, delivered before the Royal Society of Arts in 1936, stand as a classical exposition of the relation between properly constituted food and good health. Every traveller in India is struck by the contrasts in health and physique amongst her inhabitants. The Sikhs, Mahrattas and Rajputs in the Indian Army have always been splendid examples of human kind and a sharp contrast with so many of the stunted peasants of Bengal and Madras. That these differences are in large part due to the quality of the foods usually eaten was demonstrated by McCarrison in a series of experiments on animals fed on human diets. Nutrition research is too readily sidetracked into studies of the effects of a deficiency of a single nutrient upon one physiological function or anatomical structure. The reprint of these studies of whole diets on whole men and animals makes this fundamental work readily available to modern students of nutrition. In addition, there are two other essays on nutrition first published by McCarrison in 1921 and 1927, together with a modern assessment of his work by H. M. Sinclair.

Chemical Induction of Cancer. BY GEORGE WOLF, B.SC., D.PHIL. London: Cassell and Co., Ltd., 1952. Pp. xiv and 250. Figures 8. Plates 5. Price 17*s.* 6*d.*

THIS concise book, with a foreword by Professor Alexander Haddow, reviews the striking progress made during the past thirty years in the study of chemical agents that can induce tumour formation. The author is to be congratulated on the production of a most interesting and readable text on such a technical subject, and the theme can be clearly followed by those with but little knowledge of chemistry. The reviewer, a clinician, found of special interest the chapters dealing with the biological aspects of tumour induction and the hypothetical formation of carcinogenic compounds in the animal organism, and also the appendix discussing the possibilities of tumour chemotherapy. A good

bibliography follows each chapter. This book can be recommended, not only to those working in cancer research, but to all who wish for a stimulating account of this important field of experimental medicine.

Reason and Unreason in Psychological Medicine. By E. B. Strauss, D.M., F.R.C.P. London: H. K. Lewis & Co. Ltd., 1953. Pp. xii and 56. Price 8*s*. 6*d*.

Philosophically minded doctors who are interested in the fundamental logic of problems of causation will enjoy this small volume which embodies the author's Croonian Lectures for 1952 and his address from the Chair to the Medical Section of the British Psychological Society in 1946. Not the least of its attractions is a review of the rôle of psychoanalysis as a method and a doctrine. This is a scholarly exposition, to be read in a leisurely way. The reader may find the philosophical framework heavy going, but there can be no doubt about the practical implications of the author's reflections. Sir Russell Brain contributes a commendatory foreword.

Second Annual Report on Stress. By Hans Selye, M.D., and Alexander Horava, M.D. Montreal: Acta, Inc., 1952. Pp. 526. Illustrated. Price £4.

The Second Annual Report on Stress is the second addendum to Selye's large work on Stress published in 1950. That book contained 5,500 references. The first Annual Report contained about 3000 and the second contains over 4000. These figures speak for themselves. Few of us so far are inclined to accept the Selyan hypothesis *in toto*, but even those who pour scorn on the whole concept are bound to admit that it has been an astonishing stimulus to discussion and research (which is what its author, from the beginning, claimed to be its intention). 'These books are obviously not meant to be read from cover to cover' remarks Professor Selye. This remark is certainly true of the Second Report. The First Report was, as a matter of fact, very readable. The second is not. It is a carefully indexed and classified list of references with almost no reading matter. It will be of great use to research workers but to no one else.

John Abernethy. By John L. Thornton, A.L.A. London: Simpkin Marshall Ltd., 1953. Pp. 184. Illustrated. Price 25*s*.

There are two John Abernethys in the 'Dictionary of National Biography'. One (1680-1740) was an Irish dissenter of Scottish origin who was responsible for a division of the presbyterians into two parties, and also strongly opposed the Test Act, 1731. The other, his grandson, was the famous Bart's surgeon who is the subject of this short biographical study. It is probably this family background which is responsible for the grandson's curiously mixed nature—a proclivity to rudeness tempered by genuine kindness for anyone in distress. In spite of his fame—and undoubtedly he was one of the greatest surgical teachers of his time—relatively little is known about his early days and amazingly little has been written about his life. It is to rectify this omission that Mr. Thornton, librarian to the St. Bartholomew's Hospital Medical College, has prepared this new life of him. In view of the paucity of reliable information concerning his private life—he left no diaries or private papers and his family were equally parsimonious in this respect—Mr. Thornton has wisely restricted himself to a succinct summary of the available information which he has carefully sifted and confirmed. Incidentally, one of the old stories which he disposes of is that which suggested that John Abernethy the surgeon was associated with the famous 'abernethy biscuit'. According to a contemporary publication. 'At the moment the public are deceived by supposing that a certain biscuit, abhorrent to *our* olfactory and gustatory senses, was the favourite breakfast and luncheon of Mr. Abernethy, whose name it bears, because the honest baker who invented it was called Abernethy, as many of our northern neighbours are'. Mr. Thornton is to be congratulated upon the careful way in which he has collected and summarized the available facts, and his book will appeal to all who are interested in the history of surgery.

NEW EDITIONS

Medicine, Essentials for Practitioners and Students, by G. E. Beaumont, D.M., F.R.C.P., D.P.H. Sixth edition (J. & A. Churchill Ltd., 37*s*. 6*d*.). This new edition of 'Beaumont' has been pruned of a certain amount of dead wood, and has been brought up to date by the addition of much new matter. Indeed, the list of these additions, given in the preface, would provide an impressive syllabus for a course on recent advances in medicine. There are not likely to be many items relating to internal medicine that the student will seek for in vain. On the other hand, this catholicity, within the limits of so small a book, has resulted in a large number of brief notes on rarer or less important conditions, somewhat in the style of a medical dictionary. The replacement of many of these notes by more space devoted to the more important disorders would be welcomed by many teachers.

This is one of the few remaining textbooks of medicine by a single author, and as such gains from uniformity in treatment. Although not all the sections can be regarded as equally authoritative, it is an eminently sound and reliable book. The new edition should enhance the well-deserved popularity of its predecessors.

Medicine. Vol. 1. *The Patient and His Disease*, by A. E. Clark-Kennedy, M.D., F.R.C.P., in its second edition (E. & S. Livingstone Ltd., 25s.) has undergone considerable revision, with very little increase in size and only a moderate increase in price. Many of the minor blemishes of the first edition have been dealt with, but there are still too many misprints. In spite of its verbosity, it is a valiant attempt to rationalize the art of medicine. Although of little use for the junior student, the senior student and the junior practitioner will learn much from it. There is a great deal of clinical wisdom to be found in its pages.

Gynæcologic and Obstetric Pathology. By Emil Novak, A.B., M.D., D.SC., F.A.C.S., F.R.C.O.G. 3rd edition. By now 'Novak' is the accepted textbook on its subject and the yardstick by which one measures any competitors. This edition maintains the previous standard of the work (W. B. Saunders Company, 50s.). As an old friend one greets new editions as milestones in life. Happily, corpulence has not set in, for only some 25 pages have been added in spite of additional material, particularly in relation to carcinoma of the cervix and abnormalities of the placenta. A chapter on breast pathology has also been added. To the British reviewer this last might have been exchanged for more on obstetrical pathology. Dr. Novak explains modestly that he has 'revamped' his book. Actually, he must have done an enormous amount of work in this revision. As the book is an old friend so one regards some of the illustrations. Many new ones have been incorporated. One is sorry though to see that the young lady with an arrhenoblastoma of the ovary has in this edition got separated from the correct number of the illustration which should be figure 467 and not 417. Thus she acquires carcinoma of the sigmoid as an additional complaint!

The Autonomic Nervous System, by J. C. White, M.D., R. H. Smithwick, M.D., and F. A. Simeone, M.D. This third edition (Henry Kimpton, 90s.) admirably surveys the anatomy, physiology and surgery of the autonomic nervous system. The section on pharmacology warrants fuller treatment. Lewis's theory of primary vascular abnormality in Raynaud's disease is discarded in favour of abnormal vasoconstrictor activity. The authors emphasize the importance of spinal anæsthesia or procaine nerve block as indicating the results to be expected from sympathetic ablation. There is an interesting section on carotid sinus irritability and an outstanding contribution on the treatment of intractable ischæmic cardiac pain by the removal of T1-T4 ganglia. As effort ischæmia still yields painless constriction or discomfort referred to the neck (presumably *via* afferents in the vagus), there is not in fact removal of that warning which Mackenzie considered essential. Lumbo-dorsal sympathectomy for essential hypertension is advocated with enthusiasm in that group (the neurogenic), in which prognosis is often good and in which the assessment of any treatment is most difficult. The bibliography and index are good.

ALL the chapters in *A Short Practice of Surgery*, by Hamilton Bailey, F.R.C.S., F.A.C.S., and R. J. McNeill Love, M.S., F.R.C.S., F.A.C.S., have been revised in its ninth edition (H. K. Lewis & Co. Ltd., 55s.), and owing to the inclusion of new material the book has grown in volume. The number of illustrations has also grown by the addition of 135 new figures—they now total 1,234, and are notably well produced. This textbook of surgery is too well known to call for detailed comment: the new edition has been brought up to date in all sections.

Rheumatische Erkrankungen: Entstehung und Behandlung. By Prof. Dr. Max Hochrein. Second edition (Stuttgart: Georg Thieme Verlag, DM 36). This book on the genesis and treatment of the rheumatic diseases is intended for the practical physician. Professor Hochrein and Dr. Schleicher write the central and largest section on clinical and therapeutic aspects of 'infectious rheumatism', and twenty-one other contributors deal with other diseases and special aspects (teeth, surgery, radiology, dietetics, and so on). The English physician will have some difficulty in finding native nosological equivalents to 'periarthritis destruens' or 'focal rheumatism'. Treatments detailed are legion, and include spinal pumping, ganglion block, and two-and-a-half pages on calf pituitary implantation. Useful as a reference to continental practice.

The June issue will be a Special Coronation number. Particulars will be found on page lxx at the end of the advertisement section.

Notes and Preparations, see page 537
Fifty Years Ago, see page 543

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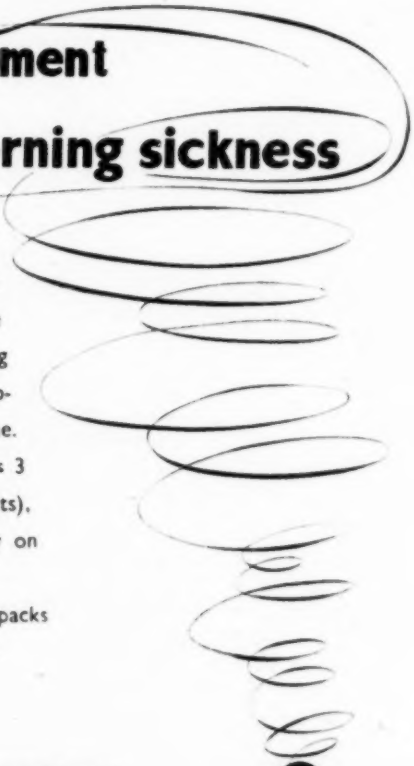

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NOTES AND PREPARATIONS

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PHARMACEUTICAL NOTES

L. LIGHT & CO. LTD. announce that their 1953 list of 'Fine Organic Chemicals' is now available. It contains over 2,300 items, many of which have not previously been available for research workers. Copies may be obtained on application to L. Light & Co. Ltd., Poyle Estate, Colnbrook, Bucks.

WILLIAM R. WARNER & CO. LTD. announce that they are the sole distributors in the United Kingdom for the preparations of Chilcott Laboratories Ltd. Two of the Chilcott preparations are now available in limited quantities: 'methium chloride' (hexamethonium chloride), and 'peritrate' (pentaerythrityl tetranitrate). (William R. Warner & Co. Ltd., Power Road, London, W.4.)

NEW APPARATUS

THE 'DAWE PORTABLE CLOSE-UP CAMERA (Type 1715)' has been designed to overcome the difficulties normally inherent in photography at close range. 'This difficult work has now been literally reduced to "pressing the button" '. The camera has the additional advantage that, as the flash bulb is completely screened from the subject being photographed, the danger of injury to the patient should the bulb burst is greatly reduced. The size of the unit is approximately 4 x 8 x 6 inches, and its weight is 5½ lb. Any standard 35 mm. film may be used. The standard lens provided is a Dallymeyer Serrac f4 5, but the unit can be adapted to other lens if required, at extra cost. (Dawe Instruments Ltd., Photographic Division, 83 Piccadilly, London, W.1.)

COLLEGE OF GENERAL PRACTITIONERS

AT a meeting of Irish general practitioners held in University College, Dublin, on March 15, 1953, to discuss the possibility of founding an Irish Faculty of the College of General Practitioners, it was agreed to appoint a committee for the purpose of making the necessary arrangements for the foundation of a Faculty, under the chairmanship of Dr. John Fleetwood. This committee will meet in the immediate future and when the necessary preliminary steps have been taken will convene a formal inauguration meeting of the new foundation. Over thirty of the practitioners present applied for membership of the College immediately after the meeting and the general consensus of opinion was that the new developments gave every promise of improving the status of general practitioners. A representative of the Irish Medical Students' Association who attended expressed the satisfaction of his group with the expressed aims of the College, and those present, that general practitioner training should play a larger part in the education of the medical student.

FIRST AID AT THE CORONATION

A COMMITTEE under the chairmanship of Sir Horace Evans is responsible for the first-aid arrangements in Westminster Abbey on Coronation Day. There are to be 25 first-aid posts in the Abbey, staffed by specialists and doctors selected from well-known hospitals. These will be assisted by nurses and St. John Ambulance men. Westminster Hospital is to be the base from which first-aid equipment will be supplied, and anyone becoming ill during the service, and requiring further treatment, will be taken to the hospital. Mr. H. E. Harding, Dean of the Westminster Hospital Medical School, is in charge of the practical preparation and running of the first-aid team.

INSTITUTE OF CHILD PSYCHOLOGY

THE annual report of the Institute of Child Psychology, Ltd. for the year ended September 1952 shows that it dealt with 161 children during the year, whose ages ranged from two to sixteen years. The vast majority of the children (111) were from state schools; 37 were from private and nursery schools, and 13 were under school

age. Asthma in children is one of the special studies of the Institute, and there were 18 cases under its care. These were all severe cases selected because of the severity and intractable nature of the condition. A special study is also being made of autistic children and childhood schizophrenia. The Institute accepts four classes of children: (i) children suffering from disturbances of their emotional life; (ii) children suffering from chronic physical disorders such as fits, asthma, catarrhs, debility, constipation and enuresis; (iii) children who are unable to adjust themselves socially at home or at school; (iv) children with educational difficulties. Mentally defective children are not accepted. (Institute of Child Psychology, Ltd., 6 Pembridge Villas, London, W.11.)

HOME NURSING IN LONDON

In 1952, London's district nurses made 1,676,429 visits—an increase of over 126,000 compared with 1951. Of this increase, about 20,000 visits were made in December as a result of the fog. To help to meet the additional cost involved in this increased demand for district nurses, the Central Council is aiming at raising more funds by collecting Queen Victoria pennies and half-pennies. (Central Council for District Nursing in London, 25 Cockspur Street, London, S.W.1.)

BCG CAMPAIGN IN INDIA

It is estimated that in India there are about 170,000,000 persons under the age of twenty years, most of whom require BCG vaccination. To tackle this problem the Government of India has entered into an agreement with the World Health Organization and the United Nations International Children's Emergency Fund, whereby WHO will provide international staff for starting mass campaigns for vaccination in the various States, and UNICEF will provide supplies, including transport vehicles and vaccination equipment. The Indian Government will provide a central BCG Organization and will distribute the required tuberculin and vaccine free of charge to the Indian States.

This agreement will facilitate the development of the mass campaign which was started in April 1951, and under which 13,100,000 people had been tuberculin tested and 4,200,000 had been vaccinated with BCG by the end of last year. The vaccine and tuberculin solution are produced in the BCG Laboratory set up in Madras by the Central Government, which is now one of the largest BCG production centres in the world, the monthly output exceeding one million doses of vaccine and 1½ million doses of tuberculin solution. In addition to supplying the material free of cost to the State Governments, it is supplied at cost price to Burma, Ceylon, Malaya and Thailand.

THE SCIENTIFIC FILM ASSOCIATION

In July the Medical Committee of the Scientific Film Association plans to publish a supplement to its Catalogue of Medical Films which was published in May 1952. Owners or distributors of films of interest to medical audiences available in this country, which are not included in the 1952 catalogue, are asked to submit details of their films if they are prepared to lend them for showing to medical audiences. The details required are: title of film, running time, summary of contents, date of production, 16 mm. or 35 mm. gauge, sound or silent, colour or black-and-white, free loan or hire, the name of the medical adviser and the address from which the film may be obtained. These details should be sent to Dr. Michael Essex-Lopresti, Medical Committee, The Scientific Film Association, 164 Shaftesbury Avenue, London, W.C.2.

NEW JOURNAL

Journal of The American Geriatrics Society, the first issue of which is dated January 1953, is to be published monthly. The editor is Dr. Willard O. Thompson of Chicago, and the associate editors include Professor L. Brull of Liége, Dr. V. Korenchevsky of Oxford, and Professor A. P. Thomson of Birmingham. The articles in the first issue include 'certain aspects of ACTH and cortisone therapy in older patients with rheumatoid arthritis', 'psychiatric aspects of mental competency in the ageing', and 'the broadening indications for tracheotomy in the aged'. The annual subscription is 82s. (Agents for the British Commonwealth: Baillière, Tindall & Cox Ltd., 7 & 8 Henrietta Street, London, W.C.2.)

HUNTERIAN SOCIETY

The Gold Medal of the Hunterian Society for the Society's Gold Medal Essay, 1952, has been awarded to Dr. Douglas G. French of Ravenswood, Kidsgrove, Staffs., and a *proxime accessit* award has been made to Dr. A. E. de la T. Mallett, of Stourfield, Wimborne, Dorset.

The subject for the 1953 Essay is 'The Management of Peptic Ulceration in General Practice'. The competition is open to all general practitioners. Further details may be had from the honorary secretary, Mr. Alec. W. Badenoch, F.R.C.S., 110 Harley Street, London, W.1.

INTERNATIONAL CONGRESS OF GYNÆCOLOGY AND OBSTETRICS

The main theme of this Congress, which is to take place in Geneva from July 26 to 31, 1954, will be prophylaxis in gynæcology and obstetrics: prophylaxis of genital tumours, and protection of the child during pregnancy and delivery. The Congress is to be preceded by an international conference on thrombosis and em-

CONTINUED ON PAGE 540

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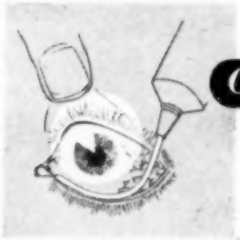

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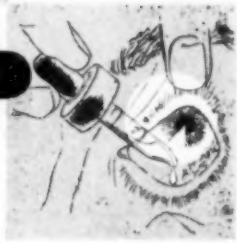

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REFERENCES

1. Paper presented before the Medical Society of the State of Pennsylvania, Oct. 19, 1950.
2. Antibiotics and Chemotherapy *1*:253 (July) 1951
3. Antibiotics and Chemotherapy *1*:146 (May) 1951.

Full literature is available and will be supplied on request

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bolism in Basle, July 20-24, 1954. (Secretariat of the Congress, Maternité, Geneva, Switzerland.)

LIND BICENTENARY CONFERENCE

IN honour of the bicentenary of the publication of James Lind's 'Treatise of the Scurvy', the Nutrition Society is holding a two-day conference in Edinburgh on May 22 and 23. The speakers will include Surgeon Vice-Admiral Sir Sheldon Dudley, Dame Harriette Chick, Professor V. P. Sydenstricker, Professor E. J. Bigwood and Dr. C. G. King.

PUBLICATIONS

Doctor at Sea. By Richard Gordon.—This rollicking, care-free tale of the sea is the ideal bedside book for the depressed doctor, and a worthy successor to the author's best-seller, 'A Doctor in the House'. Into the space of just over 200 pages, describing a voyage to South America as a ship's surgeon on the S.S. 'Lotus', the author has packed a choice selection of all the stories that were ever told about ship's surgeons and their goings on. The 'Lotus' and her crew may be 'as fictitious as the *Flying Dutchman* and her insubstantial company', but Dr. Richard Gordon has given them all the verisimilitude of life. They are just the same wonderful lot of officers and men as the reviewer sailed with as a ship's surgeon to South Africa some twenty years ago. Long may they survive. (Michael Joseph Ltd., price 10*s.* 6*d.*)

The Medical Directory 1953 is all that its predecessors have been—reliable, comprehensive and up to date. It is an admirable example of adaptation to modern conditions of life. Much water has flowed under the medical bridge during the 109 years that have elapsed since the first issue was published, but throughout this period it has always succeeded in giving the doctor the information he required in the most accessible form. Long may it continue to be the guide to the intricacies of the medical profession. (J. & A. Churchill, Ltd., 104 Gloucester Place, London, W.1, price 72*s.*)

The National Register of Medical Auxiliary Services. Orthoptists.—This, the 1953 Register of Orthoptists, is now available. It will be supplied free to medical practitioners on application to The Secretary and Registrar, The Board of Registration of Medical Auxiliaries, B.M.A. House, Tavistock Square, London, W.C.1.

Directory of Convalescent Homes, Part One, is a first attempt to list convalescent homes serving the provinces (England and Wales) which have been recommended by hospital contributory schemes affiliated to the British Hospitals Contributory Schemes Association (1948). (Royal London House, Queen Charlotte Street, Bristol, 1, price 1*s.* 6*d.*)

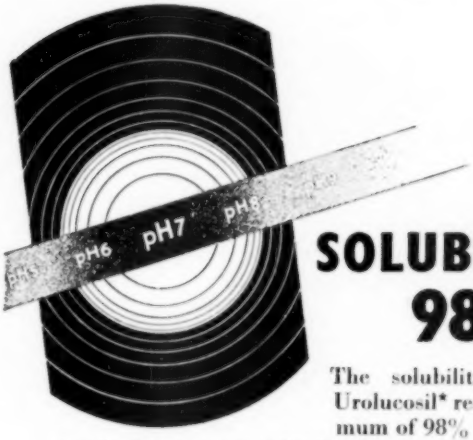
Malaria: Parasites, Transmission and Treatment is a beautifully illustrated booklet on malaria, written by three leading Dutch authorities on tropical medicine: Professor P. B. van Steenis and Dr. C. W. F. Winckel of Amsterdam, and Professor P. H. van Thiel of Leyden. Copies may be obtained on application to The London Cinchona Bureau, 10 Storey's Gate, London, S.W.1.

Gerrard The Pharmacist is a short, but interesting, account of the life of Mr. A. W. Gerrard, PH.C., one of the founders of Cuxson, Gerrard & Co. Ltd., of Birmingham. First published in the *Pharmaceutical Journal* in 1929, a second edition with addendum has been prepared on the occasion of the 75th anniversary of the foundation of the company. Gerrard, who was pharmacist at Guy's Hospital from 1862 to 1872, was an authority on the preparation of catgut (his company manufactured it under the name of 'Webb-Johnson's Catgut'). He was also the first to extract pilocarpine from jaborandi. Copies of the booklet can be had, free of charge, on application to Cuxson, Gerrard & Co. Ltd., Fountain Lane, Oldbury, Birmingham.

OFFICIAL PUBLICATIONS

Final Report of the Advisory Committee on Cardio-Vascular Disorder and Mortality Rates in Amputees.—This committee was appointed in July, 1950, '(1) to consider and advise on whether limb amputation, and the subsequent wearing of a prosthesis, can in time, produce effects on the body as a whole which may initiate or aggravate, cardio-vascular disorders. (2) To consider and advise on whether, and, if so, in what way and to what extent, the mortality rates of amputees differ, by reason of amputation, from the normal for equivalent age and sex groups'. In an interim report published in 1951, the committee reported that there was no abnormal incidence of cardiovascular disorder or hypertension among living amputees, and that the mortality rates, during 1930-50, of the total limb-wounded differed little from expectation, whether or not amputation had been performed, but in the more severe wounds and amputations the mortality rates did exceed expectation. Detailed study of death certificates during 1945-49 showed a lower mean age at death in those with leg amputations than in those with 'minor leg wounds'. In their final report the committee report that within the average figures for amputees, longevity is somewhat diminished in those who have suffered 'serious sepsis', and that in this 'serious sepsis' class there is a 'somewhat greater than normal probability that certain cardio-vascular disease will be certified as the underlying cause'. This also applies to cases of fractured femur and 'minor leg wound' which

CONTINUED ON PAGE 542



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come within the 'serious sepsis' class. Apart from sepsis, persons with double leg and above-knee amputations also experienced 'somewhat diminished longevity', compared with below-knee amputations and those with minor wounds. Two members of the committee, Dr. Hope Gosse and Dr. W. E. Lloyd, present a minority report, differing from their colleagues in these latter findings, though accepting the conclusions of the interim report.

Annual Report of the Chief Inspector of Factories, for 1951, shows that there were 828 fatal accidents, compared with 799 in 1950. The number of non-fatal accidents fell from 192,260 in 1950 to 182,616, which is the lowest recorded since 1938. Concern is expressed at the fact that, compared with 1939, there was an increase of 250 per cent. (1,756 to 6,241) in the number of accidents connected with transport. There was a gratifying drop in the number of cases of sepsis, and eye injuries were 12 per cent. less than in 1950. Young persons suffered slightly fewer accidents (11,980 in 1950, and 12,115 in 1951), but these represented a higher proportion of all factory accidents. There were 64 cases of lead poisoning, none of which was fatal. Thirty-one cases of anthrax were notified, of which one was fatal. There were 178 cases of epitheliomatous ulceration, only one of which was fatal —a record since 1920 when epitheliomatous ulceration was made notifiable. The number of notifications of chrome ulceration increased to 203, compared with 143 in 1950; the increase is attributed to the greater number of cases among workers in the manufacture of bichromate. The number of cases of industrial dermatitis voluntarily notified was 3,281, a decrease of 203 compared with 1950 (London: H.M. Stationery Office, price 6*s.* 6*d.*)

The National Health Service (*Pay-Bed Accommodation in Hospitals, etc.*) *Regulations*, 1953.—The main effects of these regulations, which came into effect on April 1, are to alter the method of calculation of hospital charges for pay-beds so as to lead to some reduction, and to authorize higher fees for certain forms of medical treatment given to private patients in National Health Service hospitals. For instance, the present over-all maximum fee of 75 guineas for operations may, in exceptional circumstances, be raised to a sum not exceeding 125 guineas, whilst the maximum fees an individual physician may charge are 40 guineas, instead of 25 guineas. The maximum fee for obstetric emergencies is now 50 guineas instead of 40 guineas, and the maximum consultation fee by general practitioner has been raised from 15 to 20 guineas. The third schedule to the Regulations contains a review of the classification of operations into the three categories of major, intermediate, and minor. (H.M. Stationery Office, price 6*d.*)

Corrigendum.—'Menstrogen' is a product of Organon Laboratories Ltd., and table 1 in the article on 'The Management of the Climacteric' in the April issue (p. 390) should be amended accordingly.

THE PRACTITIONER: 50 Years Ago. See page 543

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THE PRACTITIONER

Fifty Years Ago

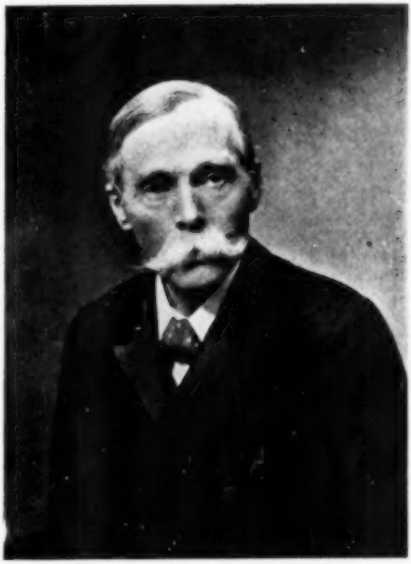
'And every tongue brings in a several tale'.—Shakespeare: King Richard *iii*, *v*, *iii*, 194.

MAY, 1903

ALL the eleven 'Original Communications' in *The Practitioner* fifty years ago are devoted to the subject of malignant disease, particularly of the tongue and lips. Walter Whitehead, F.R.C.S.ED., F.R.S.E., President of the British Medical Association, writing on 'Excision of the Tongue for Cancer', confesses to having been 'very much struck by the almost total absence of any hereditary history in the several hundred cases with which I have met. I do not think, however, that I have been successful in obtaining a trustworthy history in more than 5 or 6 per cent. of the cases which have come under my notice'. The cases which he reports 'all tend to prove that, provided the tongue and adjacent affected parts are removed thoroughly and early, there exists a fair prospect of life being extended beyond the three-year limit'. Particularly impressive is the story of a plumber in Southport, whose tongue was removed fourteen years previously and who, 'when I last heard from him two years ago, was in excellent health, and an accomplished local public tenor singer'.

Henry T. Butlin, F.R.C.S., Consulting Surgeon to St. Bartholomew's Hospital, discusses frankly 'Cases in which I have experienced great difficulty in the diagnosis of cancer of the tongue . . . in which I have myself been seriously puzzled as to what ought to be done; or in which an error of diagnosis has been made'. Sir Henry Trentham Butlin, Bt (1845-1912) was appointed assistant surgeon to St. Bartholomew's Hospital in 1880 and was put in charge of the Out-patient Department for Diseases of the Throat. Twelve years later he became full surgeon. A great authority on malignant disease and one of the pioneers in this country of the radical cure of cancer, he wrote many classic books on his specialty, such as 'Diseases of the Tongue' (1885).

In his article 'A Few Lessons from Fifty Cases of Operation for Carcinoma of the Tongue', W. H. A. Jacobson, M.CH., Surgeon, Guy's Hospital, reports the case of a former army surgeon, aged 63, whose entire tongue he had removed: 'A median scar in the floor of the mouth was all that represented the operation performed. With his artificial teeth in place . . . the patient, some few months after the operation was able to speak so distinctly as to give a most interesting account of one of the most striking episodes of the Indian Mutiny. He had been one of the surgeons in the force with which Sir Colin Campbell, afterwards Lord Clyde, relieved the garrison of Lakhnao (Lucknow). While nearing that place the English met and surrounded . . . two Sepoy regiments who were known to have murdered their officers . . . It would be impossible to have a more convincing and indubitable proof of the ability to talk without a tongue. Not only were the different details of those two fearful hours most clearly given . . . the rapidity with which retribution was meted; the sandy plain; the soldiers . . . moving about under the blazing sun from group to group of waiting dusky figures; the unshaken calm with which the Sepoys met the inevitable death; but more than this, such words as "Unao", "Bunni Bridge" . . . were perfectly intelligible'. Walter Hamilton Acland Jacobson (1847-1924), godson and namesake of



Sir Henry Trentham Butlin, Bt
(1345-1912)

Sir Henry Acland, Regius Professor of Medicine at Oxford, was appointed surgeon to Guy's Hospital in 1900. A painstaking, popular, and amusing teacher of anatomy and surgery, this 'gentle cynic' became the hero of innumerable tales and legends, even before his time.

The culpability of waiting for enlarged glands to appear before diagnosing epithelioma of the mouth is forcibly pointed out by Jonathan Hutchinson, Jr., F.R.C.S., Surgeon to the London Hospital, and son of the great Sir Jonathan, in his paper 'The Diagnosis of Epithelioma of the Mouth from Tertiary Syphilitic and Other Lesions': 'The merest tyro can diagnose cancer when such late symptoms are present, but of what use can be such a diagnosis? None of these symptoms are present in the early stage, and it is then only that a correct diagnosis may be the means of saving the patient's life. Here again, the text-book account with its table of symptoms has exercised a most pernicious effect'. 'Transhyoid Pharyngotomy' is described by Albert Carless, M.S., F.R.C.S., Surgeon to King's College Hospital; E. W. Roughton, F.R.C.S., Surgeon to the Royal Free Hospital, deals with 'The Insidiousness of Cancer of the Mouth'; and A. D. Fripp, C.V.O., M.S., F.R.C.S., and R. H. Jocelyn Swan, F.R.C.S., of Guy's, present 'Notes upon Sarcoma of the Tongue, Based on an Analysis of Forty-four Recorded Cases'.

A most interesting paper entitled 'A Further Contribution to the Distribution of Cancer', comes from the pen of D'Arcy Power, F.R.C.S., Assistant Surgeon to St. Bartholomew's Hospital: 'Like many other medical men I am interested in the increase of cancer, which has undoubtedly taken place within the last fifty years, and I have made many attempts to discover the cause. I thought, at first, that the question might be solved in the laboratory, and I spent much time in examining the various appearances which were put forward so confidently as "cancer-parasites". My distrust of the "parasites" as a cause of cancer increased on more intimate acquaintance, and ended in complete disbelief . . . But I have not yet quite lost faith in the infective or parasitic theory of cancer . . . My attention of late years has been directed more especially to places where deaths from cancer have appeared to be unduly numerous . . .'. He then gives details of two villages 'because they appear comparable with each other, and show very well the fallacies, as well as the advantages, of this method of examination. In the one set of cases the increase in cancer is real; in the other set it seems to be only apparent. Yet I may say parenthetically that in neither district would I reside . . . unless I knew that my ancestral tree was absolutely free from even a suspicion of cancer.'

W.R.B.

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JUNE 1953

GENERAL PRACTICE : TODAY AND TOMORROW

with Foreword by

THE MINISTER OF HEALTH

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